VOL.
5
60/61

Volume 5 1960–61

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VOL
5
1960/

VOL.
5
60/61

VOLUME 5

LIST OF CONTENTS

NUMBER 1

E. D. WITTKOWER: Problems in research training in psychosomatic research . . . 1
J. J. GROEN: Methodology of psychosomatic research 12
GERDT WRETMARK: Mental and psychosomatic morbidity in peptic ulcer families . . 21
J. L. GIBBONS, J. G. GIBSON, A. E. MAXWELL and D. R. C. WILLCOX: An endocrine study of depressive illness 32
Y. IKEMI, K. OKONOGI, H. DOBETA and T. HONDA: Psychosomatic research in Japan . . 42
A. J. COPPEN and A. G. MEZEY: The influence of sodium amytal on the respiratory adaptation of normal subjects 52
A. J. COPPEN and A. G. MEZEY: Metabolic effect of venepuncture in man 56
A. G. MEZEY and A. J. COPPEN: The influence of isoprenaline and prednisone on the respiratory adaptation of normal subjects 60
Book Reviews 65

NUMBER 2

J. A. STERN, G. WINOKUR, D. T. GRAHAM and F. K. GRAHAM: Alterations in physiological measures during experimentally induced attitudes 73
E. DEKKER, J. T. BARENDREGT and K. DE VRIES: Allergy and neurosis in asthma . . 83
I. COHEN, A. J. SILVERMAN, W. WADDELL and G. D. ZUIDEMA: Urinary catechol amine levels, gastric secretion and specific psychological factors in ulcer and non-ulcer patients . . 90
E. BENTAL: Dissociation of behavioral and electro-encephalographic sleep in two brothers with *enuresis nocturna* 116
J. O. SINES: Behavioral correlates of genetically enhanced susceptibility to stomach lesion development 120
L. BERNSTEIN, D. BORDA-BOSSANA, HARRIETTE ATKINSON and H. ELRICK: An experimental test of the permanence of learning deficits in the environmentally restricted rat . . . 127
C. MICHALOVÁ: The comprehensive treatment of bronchial asthma from the standpoint of corticovisceral pathology 132
Report of meeting 139
Notices 145
Book Reviews 147

NUMBER 3

J. H. REY, D. R. C. WILLCOX, J. L. GIBBONS, H. TAIT and D. J. LEWIS: Serial biochemical and endocrine investigations in recurrent mental illness 155
M. D. BOGDONOFF, M. M. BOGDONOFF and S. G. WOLF, Jr.: Studies on salivary function in man: Variations in secretory rate as part of the individual's adaptive pattern 170
B. S. HETZEL, BRIGID BRUER and L. O. S. POIDEVIN: A survey of the relation between certain common antenatal complications in primiparae and stressful life situations during pregnancy 175
R. B. SLOANE, A. HABIB, M. B. EVESON and R. W. PAYNE: Some behavioural and other correlates of cholesterol metabolism 183
G. R. FRANCOIS and J. O. SINES: Stress induced stomach lesion as related to destruction of the sympathetic ganglia 191

G. Holmberg and L. H. Beck: A systematic study of autonomic drug actions in mental hospital patients: Methodology and preliminary results 194

D. Borda-Bossana, H. Elrick, L. Bernstein and H. Atkinson: Effects of handling in the adrenalectomized rat treated with corticosterone 206

R. J. Thurrell, N. S. Greenfield and R. Roessler: The prediction of physiological responsivity from psychological responsivity 211

J. A. Stern, M. A. Stewart and G. Winokur: An investigation of some relationships between various measures of galvanic skin response 215

I. Dureman, T. Scholander and H. Sälde: An apparatus for pupillography with intermittent infrared light 224

Current Literature 227

Book Reviews 229

NUMBER 4

T. H. Holmes, Joy R. Joffe, Janet W. Ketcham and T. F. Sheehy: Experimental study of prognosis 235

H. J. Grosz: The relation of serum ascorbic acid level to adrenocortical secretion during experimentally induced emotional stress in human subjects 253

L. Goldie and J. M. Green: Yawning and epilepsy 263

B. M. Davies and J. B. Gurland: Salivary secretion in depressive illness 269

H. C. White: Hypnosis in bronchial asthma 272

P. van Wirdum and A. Weber: The occurrence of food preferences and aversions in groups of patients with peptic ulcer, asthma and neurosis 280

Current Literature 287

Book Reviews 290

Announcement 294

AUTHOR INDEX

Atkinson, H. 127, 206
Barendregt, J. H. 83
Beck, L. H. 194
Bental, E. 116
Bernstein, L. 127, 206
Bogdonoff, M. D. 170
Bogdonoff, M. M. 170
Borda-Bossana, D. 127, 206
Bruer, B. 175
Cohen, I. 90
Coppen, A. J. 52, 56, 60
Davies, B. M. 269
Dekker, E. 83
Dobeta, H. 42
Dureman, I. 224
Elrick, H. 127, 206
Eveson, M. B. 183
Francois, G. R. 191
Gibson, J. G. 32
Gibbons, J. L. 32, 155
Goldie, L. 263
Graham, D. T. 73
Graham, F. K. 73
Green, J. M. 263
Greenfield, N. S. 211
Groen, J. J. 12
Grosz, J. 253
Gurland, J. B. 269
Habib, A. 183
Hetzel, B. S. 175
Holmberg, G. 194
Holmes, H. 235
Honda, T. 42
Ikemi, Y. 42
Joffe, J. R. 235
Ketcham, J. 235
Lewis, D. J. 155
Maxwell, A. E. 32
Mezey, A. G. 52, 56, 60
Michalová, C. 132
Okonogi, K. 42
Payne, R. W. 183
Poidevin, L. O. S. 175
Rey, J. H. 155
Roessler, R. 211
Sälde, H. 224
Scholander, T. 224
Sheehy, T. F. 235
Silverman, A. J. 90
Sines, J. A. 120, 191
Sloane, R. B. 183
Stern, J. A. 73, 215
Stewart, M. A. 215
Tait, H. 155
Thurrell, R. J. 211
Vries, K. de 83
Waddell, W. 90
Weber, A. 280
White, H. C. 272
Willcox, D. R. C. 32, 155
Winokur, G. 73, 215
Wirdum, P. van 280
Wittkower, E. D. 1
Wolf Jr., S. G. 170
Wretmark, G. 21
Zuidema, G. D. 90

VOL
5
1960/

VOL.
5
60/61

VOL
5
1960/

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PROBLEMS IN RESEARCH TRAINING IN PSYCHOSOMATIC MEDICINE

E. D. WITTKOWER, M.D.*

(*Received* 14 *March* 1960)

VOL. 5 60/61

As a preamble to this paper it appears to me appropriate to define its frame of reference.

It deals with the teaching of psychosomatic research to psychiatric residents within the confines of psychiatric teaching institutions by psychiatrists and psychoanalysts in conjunction with representatives of other disciplines such as experimental physiologists, neuropathologists, internists, sociologists and cultural anthropologists. Consequently, this paper does *not* deal with the teaching of psychosomatic *medicine* or with teaching of psychosomatic research carried out operationally unrelated to psychiatry by specialists other than psychiatrists.

The enumeration of the above named disciplines implies that the term psychosomatic is not used in a narrow sense, i.e., concerning solely the mind-body relationships, but in the much wider sense of connoting a comprehensive multidisciplinary approach to problems of psychophysiological dysfunction based on a pluralistic concept of its causation.

In what follows, teachers, students and teaching of psychosomatic research will be discussed. Because the literature on the subject is minimal and because its presentation obviously should not be based on the experiences gained in one University Department, I have approached directors of research at various psychosomatic research centres and would like to express my gratitude to them for their kind cooperation.

TEACHERS

ENGEL and his co-workers (1957) have reported on their liaison program between psychiatry and medicine which has been in operation at the University of Rochester School of Medicine for over ten years. This admirable program, which arouses the envy of teachers at other universities is primarily directed towards undergraduate and graduate teaching in psychosomatic medicine. The report on it also contains significant passages on the influence of the liaison group on the psychiatric staff and on psychosomatic research.

As regards teachers in this area, ENGEL and his associates postulate that they should have a foot in both camps because psychiatric teachers fail to function as models for identification if, without solid grounding in medicine, they expect their students to view the patient "as a whole" though they are unable to do so themselves. This argument, which is undoubtedly of utmost importance for undergraduate teaching, is less valid for teaching of psychiatric residents: (a) because they have already identified themselves with psychiatry; (b) because, as ENGEL points out, the complexity

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of modern medicine is such that no single person can encompass all its aspects; and (c) because, at any rate, psychosomatic research necessitates a team approach. Hence though a thorough knowledge of the borderline area on the part of the teaching psychiatrist is undoubtedly highly desirable and goes a long way in facilitating successful cooperation, the main prerequisite of combined teaching and research in teacher as well as students seems to be the capacity to function as a member of a team, i.e. to tolerate view points different from his own and to integrate conceptually observations made from various angles. This, of course, is equally true of all interdisciplinary research.

STUDENTS

There is a grave and deplorable shortage of psychiatric research workers. This shortage has been attributed to the discrepancy between financial rewards for the research worker and for the clinician; to the absence of unified theory of human behaviour; to the "unreality" of psychiatric verbiage; to undue emphasis on applied research; and to the initiative- and creativity-stifling bureaucracy of some research sponsoring and supporting agencies and authorities (RUESCH, 1957). Other factors which may be considered are: the scarcity of available training centres in psychiatric research; the specific difficulties inherent in psychiatric methodologies; the teaching of psychiatry on the model of and with the specific goal of private practice; the length of time required for psychiatric training; and the therapeutic urge of many young psychiatrists not infrequently arising from their own emotional difficulties. The residents' primary concern is, of course, to obtain their board accreditation, to become competent clinicians and, if they are married, to support their families. But this does not mean, as GRINKER has pointed out, that their research proclivities need be discouraged by clinicians who adopt a depreciatory attitude towards laboratory studies, or should they undergo psychoanalysis, by the attitude of some analysts who believe that research interest outside the analytical situation is a neurotic manifestation.

To counteract this trend it has been suggested that interest in research in general and in psychosomatic research in particular be stimulated on the undergraduate level. Referring specifically to psychosomatic research GRINKER writes: "We will have to extend ourselves further back into the medical schools and attempt to keep alive the spirit of curiosity in the few dedicated people who might advance our field."

It is obvious that more than others, students are likely to be interested in psychosomatic medicine and psychosomatic research at those medical schools at which one of their teachers or several teachers are specifically interested and engaged in psychosomatic research, at which liaison between the Department of Psychiatry and other clinical Departments is close, and at which elaborate teaching programs are carried out at the undergraduate level in close cooperation between the respective Departments. Without going into details of differences in psychosomatic training of medical students at various universities which would go beyond the scope of this paper, reference may be made to the participation of medical students in psychosomatic research both during the summer and during the school year within the framework of ENGEL's liaison program at Rochester and as part of the extensive research teaching program of Levine at Cincinnati which will be described at some length later on.

Despite an extensive teaching program in psychosomatic medicine for medical

VOL
5
1960/

students at our University and despite the fact that several members of the teaching staff of our Department present to our students the model of individuals who have devoted a great deal of their lives to psychosomatic research, the number of postgraduate students specifically interested in this area is small—not more than 1 in 10 and probably 1 in 20. The percentage reported from Cincinnati—15 per cent—is roughly the same (GOTTSCHALK).

By and large, postgraduate students who show an interest in research are in our experience a cut above the average. They often combine a reasonably strong clinical interest with a critical attitude towards current psychiatric formulations resulting in a healthy curiosity to find out for themselves. Interest in the *subject*, i.e. a true scientific interest, may prevail over interest in the *object*, i.e. a therapeutic orientation. As far as psychosomatic research is concerned, they obviously aim at encompassing and linking up the concepts of at least two adjacent disciplines.

Roughly they fall into two catagories: (1) those interested in a career as teachers and investigators, and (2) those wishing to widen and to enrich their psychiatric experience and knowledge by a year of research carried out under supervision.

As stated before, the number of those who contemplate, and are actually suited for, an academic career is lamentably small. By far the majority of postgraduate students interested in research, in our experience and in that of others, belongs to the second category. To the two groups named, unfortunately, a third small group must be added, made up of those who wish to take a year at a somewhat higher pay than usual.

Measures taken or advocated to attract students to research and to build up a body of research workers in our field include the following:

(1) Participation of medical students in psychiatric research projects.

(2) Stimulation of some residents to engage in part-time research before they commit themselves to full-time private practice.

(3) Encouragement of students to spend one year of their Diploma course on research (at our Department the 3rd or 4th year of the Diploma Course).

(4) Scrutinizing of residents during their training for the possibility of applying for career grants for some of them and to incorporate others directly in the staff of the Department.

(5) Setting-up of a separate type of residence for research-oriented people in which there is less clinical activity, teaching and experience but enough to prepare the individual for his Board examinations (GRINKER).

(6) Encouragement of the mastery of a second discipline, e.g. the taking of a higher degree in physiology, psychology or sociology (CLEGHORN).

(7) Establishment of stimulating teaching programs, in psychosomatic medicine on the undergraduate as well as on the postgraduate level.

TEACHING

Questions which come to one's mind are: *Can* research be taught? *Should* research be taught to psychiatric residents? And, if so, *how* should it—and *what* should—be taught?

(1) *Possibility of teaching research*

The obvious answer to the first question is that research can *not* be taught but that a research orientation can be inculcated in the minds of young physicians.

(2) *Advisability of teaching psychosomatic research*

While hardly anybody will dispute the value of exposing undergraduate students and especially postgraduate psychiatric students to a comprehensive, holistic and integrative approach to health and illness, the question whether systematic teaching of research in general and of psychosomatic research in particular should be a compulsory part of the curriculum of psychiatric residents is debatable.

Those who favour courses in this area emphasize the necessity to train young psychiatrists in the principles of rigorous scientific thinking. Thus one of my correspondents, an internist, writes: "I am continually impressed by their complete lack of critical faculties and their lack of recognition of the basic tenets of research. Their innate curiosity seems to be directed more toward concepts and symbols than to the usual sublimation seen in internists and basic scientists where the basic concern is for the mechanisms of disease processes" (LACHLAN WHITE). WHITE's argument is in line with that of GOTTSCHALK who, representing the Cincinnati School states: "We feel that *all* of our residents, though they may not have any incentive to do research, must learn how to evaluate the meaning and clarity of psychological and biological concepts, what is the experimental method, the natural history approach, the adequacy of sampling procedures and controls."

Likewise the wisdom of impressing a research orientation on students is stressed by GRINKER who writes: "The attitude of this Institute is one of questioning and doubting, taking nothing written by authorities for granted. There is a constant discussion of validity of concepts, and education is directed to more than experience in psychotherapy. We attempt to inculcate the notion that there is more to the role of a psychiatrist than that of a psychotherapist. We attempt to indicate clearly that psychosomatic is more than a concept applicable to only sufferers from physical disturbance but that it is a generalization applicable to all medical and psychiatric illnesses."

Others, by contrast, stress that teaching of research (of whatever kind) should not be imposed on residents: (a) because, in view of their therapeutic orientation, with few exceptions, interest in research is lacking (LHAMON, HOLMES, FINESINGER, CLEGHORN); (b) because even genuine scientific curiosity can rarely be maintained owing to the pressure of clinical work (MALMO); (c) because few can mix research with all the other techniques and new information that needs to be mastered (CLEGHORN); and (d) dealing specifically with psychosomatic research "because in general most psychiatric residents do not come with the degree of experience in and knowledge of organic disease and physiologic and biological processes to equip them to do research in many aspects of this area." (ENGEL).

Consequently there are few universities at which a formal course on psychosomatic research is run. As LOVETT-DOUST puts it: "We run no formal teaching course on psychosomatic research as such because we feel that the research potential of postgraduate students can best, and perhaps can only, be served by a wide survey of the horizons of existing knowledge, and the provision of facilities and encouragement to probe these horizons." Writing in a similar vein ENGEL states: "Even in the Fellowship program I have not made research interest or participation a requirement. In fact this is based on my feeling that research talent is a highly individual and not too common quality and that there is no advantage in encouraging people to do research who basically do not have the talent nor the inclination."

VOL
5
1960/

To these arguments, that of KUBIE may be added who underscores the considerable hazards to which young psychiatrists are exposed when prematurely plunged into research. Briefly, these consist of the necessity to swallow large portions of working hypotheses, blind faith in techniques they have no time or skill to question, and over-identification with the prejudices and biases of the older men for whom they work.

The view seems to prevail that inculcation of research orientation in undergraduates and postgraduates is desirable, that facilities should be offered and encouragement be given to residents who show interest in research (psychosomatic or other) but that coercion of those who lack interest in research and are unwilling to learn about it bears little fruit.

(3) *Teaching procedures*

Research is by no means universally taught to psychiatric residents at North American universities. In some departments, such as ours, scientific methods are taught with due regard to psychosomatic research but not specifically confined to it. As mentioned before, there are very few centres at which a specific psychosomatic research training program has been developed.

An outstanding example of these is the Department of Psychiatry of the University of Cincinnati. The research teaching program at this University, as also mentioned before, starts with the medical students and comprises a program for sophomore and junior medical students, generally during the summer session, for selected students awarded Public Health Service stipends. Students attend relevant sessions of orientation lecturers for new residents, and they are assigned to a member or members of the Staff to work on research projects. The students may work on a project of their own choice, if after a discussion with a Staff member the project is approved; they are also assigned a research project or are invited to join as a member of a research team of some departmental ongoing research. The teaching is carried out completely on a tutorial basis under the primary guidance of the Staff member to whom the student is assigned. Extra conferences and seminars with other Staff members are arranged as need arises. The Department includes a full-time research teaching member, Dr. Goldine Gleser, who is an Associate Professor of Psychology in the Department and whose specific job is to teach and advise on research design, the mathematical evaluation of experimental data, controls, sampling procedures, and so forth. Also during the sophomore year of medical school, a team of teachers including psychiatric residents and Staff, under the aegis of Dr. Martin Macht, an internist and also a Ph.D. in physiology, take a course on psychophysiology in which they run experiments in this field. A discussion of psychophysiological relationships is a central part of this course.

An attempt is made by various means to stimulate the interest of all psychiatric residents in research approach, objectives and procedures. In weekly diagnostic and psychotherapeutic conferences with Dr. LEVINE and other members of the Staff, the residents are taught to strike a balance between the imaginative and speculative processes of fact-finding and the testing of the reliability and validity of working concepts and tentative hypotheses. Furthermore, a short series of didactic lectures is given, for all residents, detailing the fundamental characteristics of the scientific method, the types and stages of research, the ways of describing variables (central tendency, range of variation, correlation, methods of assessing differences and so

VOL.
5
60/61

forth). Furthermore, during each tour of rotation by a resident through the psychosomatic service, an attempt is made to assign a short research project involving psychophysiological variables. Because of the pressure of other activities it is not always possible to do so.

Special encouragement is given to residents who spontaneously show interest in learning about and doing research. Again, the principal method of teaching is through individual discussions with Staff members and actually becoming involved in research activities. Many of them become integral members of a research team or carry on independent research that is worthy of publication. These residents are invited to attend monthly Staff research seminars held in the evenings at the homes of Staff members, where research ideas and results are thoroughly discussed. Also, quarterly research seminars, primarily for the residents, are held where their research activities are presented.

GOTTSCHALK who reports on this program sums up its principal features as follows: (a) there are some minimal requirements for all residents, but principal energies are spent on residents showing spontaneous research interest and aptitude; (b) main teaching procedure is tutorial and on an individual basis, as well as having the resident get involved in a research activity; (c) some didactic sessions are given on a group basis for all residents, somewhat more such sessions for the residents interested in doing research; (d) all these didactic group sessions will be increased in the coming year.

The program just outlined throws into relief the three teaching procedures generally used. (1) Lectures; (2) Seminars; and (3) Research under supervision.

(1) *Lectures*

Most teachers will probably agree that lectures on research *per se*, i.e. without concomitant practical research experience, are of little value. The necessity to give ample time for discussion at the end of each lecture has been stressed.

Psychiatric residents are apt to consider any subjects which they regard as peripheral to psychiatry as unessential and to become bored on being presented with them. Thus CLEGHORN reports that a course on the Psychosomatic Aspects of Endocrinology which he gave some years ago did not prove popular—"In part because few of the residents have had as much endocrinology as McGill students and there is a relative lack of interest in something which appeals to them as being a bit removed from psychiatry."

As regards *content* of lectures, the areas covered in didactic sessions at various centres more or less correspond to those outlined by Gottschalk in his description of the Cincinnati program though they obviously vary to some extent with the specific research interests of the teachers concerned.

SHAGASS presents his thinking on the subject, i.e a classification of content of lectures, as follows:

(a) *Theoretical framework and approaches.* This would include consideration of the concept "psychosomatic" and the various theories and approaches. He states: "I prefer to include a specific discussion of field concepts, as opposed to "class" concepts. Such approaches as the transactional can then readily be fitted into field theory."

(b) *General methodology:* (i) Criteria of proof as applied to psychosomatic

VOL
5
1960/

relationships, including the problems involved in interpreting causation. How these may influence research design. (ii) Statistical method in relation to (i). (iii) Problems of the control group, the representative sample etc. (iv) The proper statement of a research problem as a key step in research. This involves not only an interest in a problem, but an understanding of pertinent knowledge, its relation to general theory, and a grasp of appropriate methods for obtaining relevant new information.

(c) *Specific methodology*. The fields to be covered would be many: psychology, psychiatry, sociology, cultural anthropology, biochemistry etc. One way of doing this would be to select one example of research utilizing the specific methods of each field to be covered, such as Wolf's work on Tom for gastric physiology.

Another aspect of methodology, if not adequately covered elsewhere, would be to consider the various psychological approaches that have been used in relation to physiology, i.e. cross-sectional and longitudinal personality study, psychotherapy, stress interview, experimental stress, etc. Margolin's physiological and psychological studies using the technique of psychoanalytic interviews on a 22 year old single Negro girl with a large gastric fistula and Engel's and Reichsman's study of Monica are excellent examples of integrated observation at several levels.

(d) *The final session or sessions* might be devoted to a further attempt to formulate a general "psychosomatic" point of view, in the light of the previous discussion. SHAGASS states: "This supplementary orientation is often neglected, on the implicit assumption that it has already been adequately covered earlier. In making this assumption the teacher forgets that he arrived at his own point of view only after considerable work and time, and that his students will also require time."

GRINKER utilizes a course of psychodynamics to expound the psychosomatic model. He also gives a course on the biological basis of psychiatry assisted by a fairly large multidisciplinary team of researchers including biochemists, endocrinologists, experimental psychologists, psychophysiologists, clinical psychologists, and psychiatrists.

H. M. FOX is about to start a series of four lectures on psychophysiological research methods to the psychiatric residents at the various Harvard hospitals. This is part of a more general postgraduate course of psychiatrists which includes lectures on basic psychological concepts, including such topics as Psychoanalysis as a Developmental Theory; Structure, Energy and Content; Instinct Theory; Early Childhood Development, etc.

He is planning to give an initial lecture on Ego Function and Homeostasis based on his own well known work—as an illustration of methods which might be used for the establishment of tentative hypotheses concerning the relationship of ego function to physiological homeostasis.

Ben Murawski, the chief psychologist at the Peter Bent Brigham Hospital, has been asked to give the second lecture describing some of the statistical methods needed for these studies. He will include presentation of the concept of standard deviation as well as the use of coefficients of variation and also methods for the study of groups, such as the Analysis of Variance using his observations on flicker fusion to bring out ways in which the successive observation on an individual can be compared to variations between individuals who are members of the group under study.

D. Nelson, Chief of Dr. Thorn's metabolic laboratory, has been asked to give the third lecture. Nelson will present those aspects of endocrine balance which reflect the

adaptation of the organism to stress and will specifically describe the responses of the pituitary-adrenal system as an illustration. He will include information about what is known concerning the physiology of the pituitary-adrenal responses and also something about methods of measurement, such as the ACTH test, and the kind of information that would be needed to interpret the meaning of blood and urinary steroid levels.

D. Funkenstein will give the fourth lecture during which he will present some of his concepts concerning methods for correlating certain types of personality make-up with measurable indices of neuroendocrine response.

(2) *Seminars, research conferences*

By and large research seminars are preferred to set lectures as a teaching procedure.

Two types of seminars are run: (a) those starting off with published papers attempting to find out the assumption, questions, hypotheses and research designs which the authors used; and (b) those concerning research projects in which the students participate or which they intend to set up. In either case the research topic chosen is used as a focal point for discussion of scientific method as well as theory.

ENGEL recommends to students, who express interest in research, attendance at and participation in research conferences at which both general concepts and specific research methodology are discussed, usually weekly. In addition, he urges them to continue to pursue assidiously their clinical work with patients on the wards and clinics since this provides an essential background for their knowledge of patients with somatic disorders and for the methods of obtaining data on such patients. They are also encouraged to observe ongoing research projects and to discuss the projects with the participants, as well as to consider projects of their own.

(3) *Research under supervision*

The amount and nature of research carried out by residents varies from department to department. As mentioned before, it depends on such factors as acceptance of the psychiatric department by other departments, its prestige, the research interests of psychiatric teachers and teachers in other specialities and disciplines, their personal relationships and the research orientation—versus helping the poor, sick and needy—as a whole.

MARGOLIN specifies the following conditions as limiting factors: (a) a resident with a "research attitude and/or history"; (b) a preceptor with active research programs; and (c) clinical and laboratory facilities. Of these three conditions, he regards the human factors as the most important, and the facilities as the least important.

There is probably a consensus of opinion that the tutorial procedure—what MARGOLIN calls preceptorship—is the most effective teaching procedure in both initiating a project and supervising it afterwards. The role of the supervisor, as I see it, is to provide facilities, to iron out difficulties, to assist in research design and interpretation of data, to maintain interest and to allay anxieties whenever they arise. He should encourage and guide rather than instruct or direct.

One's understandable tendency as a research supervisor, is to employ research students in one's own area of interest and, indeed they often ask for research suggestions or to join ongoing research projects. By and large, in my opinion, employment of research students in projects other than their own hampers their initiative, creativity and originality.

VOL. 5 1960/6

My own practice in dealing with students who wish to do research under my supervision, is to explore the areas of their specific interest and to help them to develop their ideas and suggestions as far as is possible. Once an area of interest has been defined and tentative working hypotheses have been developed I then ask the student to prepare a memorandum stating explicitly his research objectives and research design.

Obviously much time has to be spent, in the initial stages, on setting up the project and on techniques to be employed. For instance if interviewing of patients is the major investigative technique employed I make a point of interviewing patients in the presence of the students and demonstrate my own method of recording material obtained. Should the cooperation of representatives of other specialties or disciplines be required lengthy discussions between all the participants precede the actual research. Throughout the whole project tutorial sessions are held at regular intervals concerning methodology, change in procedure, analysis of data and final write-up.

In addition research conferences and colloquia have proved useful to us and others as a procedure of guidance. For instance, once a research proposal submitted by a resident has reached a level of organisation which indicates some promise and practicability, ENGEL and his associates take it up at one of their research conferences for a full dress discussion. Such meetings may occupy anywhere from one session to as many as half a dozen before the problem has been adequately considered. The main function of these conferences is to provide an opportunity for the proponent and for the audience to consider all the many aspects of method and design. The administrative decision as to whether the project will be initiated and supported rests in the hands of a much smaller group. The nature of the subsequent research experiments, according to Engel, depends on the nature of the problem. In general the investigator is asked periodically to review his progress at the research conference.

Difficulties encountered. Surprisingly few of my correspondents have given consideration to the difficulties which undoubtedly exist in the research training of psychiatric residents.

Time. One would certainly agree with MARGOLIN that the resident's motivation must be very high, that the preceptor must be quite inspiring and that the house staff on the services must be indulgent and interested, to allow the resident to do research despite a demanding service and training schedule.

But even if, as in our Department, a year of the Diploma Course can be put aside for research, the time pressure is considerable. It takes about three months to overcome initial difficulties—to learn laboratory techniques (in laboratory research) and to establish a steady flow of patients (in clinical research). Then the research proper starts, yet by the time it is well under way the resident has to break it off because he requires at least three months to analyse his data and to write up his findings.

Money. Every research director knows the predicament of either having funds but no suitable research worker, or of having a suitable research worker but no funds. To raise funds takes time and is difficult if the investigator has had little or no previous research experience. Hence it may occur that by the time research funds have been procured the resident has been compelled by the uncertainty of his situation to accept another job.

Engel has made it a point to secure funds in his department which can be used to finance very early research projects at the prepilot or pilot stage. He states that "since it is virtually impossible to secure money on short order for an unknown investigator, the availability of such money makes the difference between whether or not the research can be started at all."

Other handicaps. Other difficulties encountered by psychiatric residents engaged in research include:

lack of experience in clinical medicine, physiology and biology as far as the somatic aspects of the problem are concerned;

lack of experience in dynamic psychiatry as far as the psychological aspects of the problem are concerned;

disinclination to do laboratory research owing to predominance of interest in clinical psychiatry;

therapeutic involvement with individual patients instead of concentration on the research problem;

disillusionment and boredom after the initial fervour has worn off and the donkey work of collecting a sample big enough to be of statistical value has started;

tension and anxiety aroused by enforced breakdown of segregating barriers between well defined disciplines;

difficulty in making, reporting and recording observations;

reporting of observations in minute detail without being able to separate the wheat from the chaff or to see the wood for the trees;

interference of collaborating physicians other than psychiatrists higher in professional status;

difficulty in structuring the data obtained and to arrive at generalizations and theoretical formulations; and

deficiency in writing good English so that the supervisor may find himself faced with the cumbersome task of having to rewrite from beginning to end a lengthy article written in atrocious English.

Results obtained. There are, of course, known to all of us some shining examples of young men and women who discovered their vocation as career research workers during their residency. But more often than not, research interests evaporate and the lure of private practice prevails.

In all fairness, one should hardly expect more from a resident than a solid data-collecting job and should, in our view, regard his venture into research rather as research training than as research. As such, research experience certainly serves a useful purpose. But with few exceptions no papers worthy of publication should be expected or aimed at.

Beyond this, looking back at nearly 30 years of experience as a teacher of psychosomatic research, I am reminded of Oliver Wendell Holmes' division of minds (quoted by FULLER ALBRIGHT) into "one-storey intellects, two-storey intellects, and three-storey intellects with skylights." "All fact collectors," he noted, "who have no aims beyond their facts, are one-storey men. Two storey men compare, reason, generalize, using the labours of fact-collectors as well as their own. Three-storey men idealize, imagine, predict: their best illumination comes from above through the skylight." There are many buildings of considerable height, but three-storey intellects are uncommon.

VOL.
5
1960/6

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METHODOLOGY OF PSYCHOSOMATIC RESEARCH*

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INTRODUCTION

THE triumphal advance in medicine during the past century is to a large extent due to a methodology which is based on the assumption that the human organism in health and disease can be studied and understood as a chemical, physical or biological system. In this concept the mental life of the individual and its disturbances were kept out of the field of vision of the scientific investigator and delegated to intuition or philosophical reasoning. However, the conviction has been gaining ground that this scientific simplification of man, although it has served a useful purpose, is no longer tenable. Whereas the physicochemical and biological approach achieved great advances in our knowledge of the infectious, metabolic and endocrine disorders, it neglected the problems of mental disease. Moreover, a number of organic diseases, and among those some very common ones, such as ulcerative colitis, peptic ulcer, essential hypertension and bronchial asthma, have remained resistant to all attempts to clarify their etiology by physicochemical or bacteriological methods. Clinical observation, however, seems to indicate that the emotional life of the individual plays an important role in the causation of these disturbances, and psychiatric studies, carried out in patients with these internal diseases, revealed the presence of neurotic traits and conflicts in many of these individuals. As a result of these clinical and psychiatric observations a number of far reaching hypotheses have been formulated, all of which seem to agree that, although they differ in detail and terminology, these severe organic disorders are primarily of psychogenic origin. A large part of what is now called psychosomatic medicine consists of these psychiatric observations and hypotheses.

This situation confronts the modern physician with a methodological problem. As a scientist he is accustomed to deal critically with observations of doubtful exactitude and significance, and a hypothesis to him has the meaning of a systematized supposition which can be put to the test by a critically arranged experiment. This attitude seems irreconcilable with many of the observations and hypotheses with which he is confronted in psychosomatic medicine. The facts on which the hypotheses are based are often not more than clinical impressions, obtained without systematic research and without adequate controls, or they are the results of introspection and intuitive communication in which the personal errors of patient and observer are obviously very large. Many hypotheses are built on psychoanalytical or phenomenological concepts and deductions; they are expressed in terms which are insufficiently defined or not operational within a scientific frame of reference. They do not lend

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VOL.
5
1960/6

themselves therefore to testing by any of the methods which the clinical investigator has at his disposal. Nor yet can he refute them, so that the problem presents a perpetual challenge.

In this dilemma two ways seem to be open for the further development of psychosomatic medicine. In the first, one admits that the medical approach to man and his disease up till now has been too one-sided and that as man can never be completely understood in a purely biological framework, doctors who are interested in a complete understanding of their patients must change their attitude. They have to adopt "das einfuehlbare Verband", "die Begegnung", and the analysis of the "Dasein" in their approach to patients. In this approach, methods like psychoanalysis or existential analysis are just as legitimate as the culture of bacteria or chemical analysis in a biological frame of reference. The second school of thought maintains that even if the biological study of man has till now been one-sided, this would equally be the case with a purely psychological approach. According to this line of thought man in his completeness can only be understood by an integration of different points of view, each, however, working within its own frame of reference. The systems of reference complement each other, but each is legitimate within its own framework. In this concept it is equally possible to study psychosomatic problems within a scientific as within a phenomenological framework. The over-simplification of the past century overlooked the fact that mental phenomena also belong to man as a biological and social being. They also occur in animals, albeit in different manifestations. The scientists' fault has been that they were frightened by the *word* "psyche" and were held back by the pre-conceived idea that science could not contribute to an understanding of mental processes, although this pre-conceived attitude itself was unproven and unscientific. If we assume that mental processes are the subjective experiences of what goes on inside the brain and in the outside behaviour of and between individuals, psychosomatic phenomena become available for scientific methods by the study of their objective manifestations. In a scientific framework it is not the psyche, but the central nervous system, and the behaviour of organisms in their environment which need and can be studied. Psychosomatic medicine can be approached scientifically via the biological study of neurovisceral interactions, and the sociological study of inter-individual relations and behaviour.

In this paper we will concern ourselves with some methodological problems of psychosomatic research within such a scientific framework. We wish to repeat that this methodology claims no superiority over the psychological approach, but is in no way inferior to the philosophical or psychological views on man and his diseases.

PSYCHIATRIC STUDIES

When the psychosomatic research group in the Wilhelmina Hospital in Amsterdam (GROEN, 1957a) was founded in 1947, the problem of its methodology immediately came up. Its first steps certainly differed in no way from the psychiatric approach as used elsewhere. The results of interviews with the patients were interpreted by the psychiatrist Dr. Bastiaans, using psychoanalytical concepts, and hypotheses were then formulated. The physician (J. Groen), introduced the method of *biographical anamnesis* in an attempt to objectify the psychiatric method, although fully aware that he was still using a method with a large subjective error. As a result of this largely psychiatric approach, the first communications of the research group offered

little more than hypotheses concerning psychosomatic relationships in ulcerative colitis, peptic ulcer, bronchial asthma, hypertension, etc. (GROEN, 1951, 1957). These hypotheses were perhaps formulated in more simple language coming from a department of medicine, but they were fundamentally not different from the hypotheses of Murray, Alexander, Flanders, Dunbar and others.

In this state of affairs two steps were taken which subsequently proved to be of value in the building up of a more systematic methodology for psychosomatic research.

PSYCHOLOGICAL STUDIES

The first step came through the work of the psychologist, Dr. Barendregt, who pointed out that many psychological tests, especially those requiring subjective interpretation by the psychologist, suffering from the same drawback as the psychiatric method itself, namely a high and unknown degree of subjectivity. Against this the following principle was adopted:

We divided our psychiatric hypotheses into those which we termed fruitful and (at least for the time being), unfruitful. Under fruitful we subsume a hypotheses which: (a) is formulated in terms that can be understood and used by workers from different fields, and (b) allows the hypothesis to be tested by the application of a method independent of the one by which it was arrived at. By this we meant that for a psychiatric hypothesis to be fruitful, it would have to lend itself to be tested either by an independent psychological or a physiological method, and vice versa. It was in the testing of these fruitful hypotheses by independent and validated tests that the psychologist found his main task.

Of the work which was done along those lines we mention Barendregt's testing of the hypothesis of the psychosomatic etiology of some disorders. In some of their earlier papers Bastiaans and Groen had formulated the hypothesis that psychosomatic patients were actually neurotics, who differed from the 'openly complaining' psychoneurotic patients proper in a strong tendency to inhibit such neurotic behaviour patterns as compulsions, complaining about anxiety, crying, shouting, asking for help, or making excessive demands on the doctors' time and patience. Barendregt deduced from this hypothesis that if a number of psychosomatic patients from the department of medicine (and he chose for this purpose patients with peptic ulcer and asthma), a number of psychoneurotic individuals from the department of psychiatry, and a healthy control group, were given the Maudsley test for neuroticism, there should be no significant statistical difference between the neuroticism score of the psychosomatic and the psychoneurotic patients, who would, however, both differ significantly from the score of the normals. On the other hand, when the same three groups were given a test for 'sociability' it was predicted that the psychosomatic patients—because of their strong tendency to behave like normals—would not significantly differ from the healthy group, whereas the other group would. (For this last test a modification of Eysenck's test for extraversion–intraversion was chosen.) The results confirmed all predictions with a high degree of statistical significance, and thus a psychiatric hypothesis based on biographical anamnesis and on a few psychoanalysed cases was supported (BARANDREGT, 1958).

It is obvious that a large field opens up here for clinical psychology in which this science (provided it can make its validated methods truly independent) can play a

VOL.
5
1960/6

large role by putting our knowledge about man's mental processes in health or disease on a scientifically firmer basis, by supporting some psychiatric hypothesis and by not supporting, or rejecting others.

PHYSIOLOGICAL STUDIES

The second important contribution towards an objectivization of our researches came from the contact with H. G. Wolff, S. Wolf and their group in New York. Their work on Tom, the man with the gastric fistula, demonstrated that the stomach reacted to emotional stresses in a similar way as it did to local chemical and physical stimulation (WOLFF and WOLF, 1955). This work, however, was not only important in providing valuable support for the hypothesis of the psychogenic etiology of peptic ulcer, it meant also a tremendous step ahead in the methodology of psychosomatic research in general. WOLFF's method was based on the assumption that a hypothesis about the psychogenicity of a disease can be supported by physiological observations, if the reproduction of an emotional situation under controlled laboratory circumstances, produces such similar bodily changes in the acute experiment as are chronically present in the diseased individual.

This physiological approach to the study of psychosomatic disorders has already borne rich fruits. During the past years WOLFF and his associates have systematically applied their method to the study of the behaviour of the colon, the mucous membrane of the nose, the urinary bladder, the blood pressure and the blood sugar and ketone bodies, under the influence of experimentally induced emotional conflicts (WOLFF *et al.*, 1950). In Amsterdam VAN DER VALK has similarly studied by continuous registration the behaviour of the electrical resistance of the skin, the sweat secretion, the skin temperature, the blood pressure, and of some other variables during emotional interviews and during what we designated as experimental self-control. This was achieved by bringing the individual into, for him, unknown surroundings (the laboratory) and there asking him not to speak and not to move while the physiological registrations were carried out (VAN DER VALK, 1950, 1958).

In another study carried out with DEKKER, a situation was reproduced in the laboratory which, according to the patient's history, had induced asthmatic attacks in him. In this way it was shown that asthmatic attacks can occur in situations which have a stressful meaning to the patient and where allergic influences could be excluded with practically complete certainty (DEKKER and GROEN, 1956).

The physiological method, however, is not only a valuable means of putting certain psychiatric hypothesis to the test. It enables us to study the physiology of emotion as such and to deduce from this study physiological hypotheses. Thus H. WOLFF's group and our group independently formulated the hypotheses that many so-called psychosomatic disorders are the result of reaction patterns (such as a rise in blood pressure, in blood sugar, in secretion of gastric juice, in intestinal motility) which are regularly observed in normal individuals and therefore must be regarded as belonging to the natural behaviour of the organisms in certain situation. These, in themselves normal patterns, however, become disease-producing mechanisms when they occur in abnormal duration and intensity. This hypothesis has prompted further research into the question why some individuals, even if they are 'qualitatively' normal, react in this quantitatively exaggerated way (WOLFF *et al.*, 1950; WOLFF, 1951; GROEN *et al.*, 1953, 1957).

ANIMAL STUDIES

The clinical investigator often derives great benefit for the elucidation of human disease from the study of animals. Animals can be bred in such a way that they become genetically almost identical, they are available in large numbers, and the investigator is less limited in the scope of his experimentation, than in the case of human individuals where the ethical code of his profession forbids him to carry out an experiment which might do harm to the wellbeing of a patient. It is obvious therefore, that much useful knowledge could be obtained if we could produce and study psychosomatic disorders in animals. Two factors have held back progress in this field until recently. The first factor was the attitude of many psychiatrists that the human psyche is a unique phenomenon, which is fundamentally different from what is studied in so-called animal "psychology", so that results obtained in animals will never be applicable to the understanding of the psyche of man. The second objection maintained that it would never be possible to produce in animals the same complicated feelings of rivalry, humiliation, love loss, etc., that seem to play a role in the etiology of some psychosomatic disorders in man.

As far as the first objection goes, we seem to be dealing with a preconceived axiom, rather than with an objective statement of fact. Even if one does not deny that religious experience, rational reasoning and linguistic expression are specifically human, it would be hard to prove that higher organized animals, although they cannot experience religion and cannot express themselves in language, are also unable to experience something comparable to certain of the nine simple human feeling states. The reactions of animals following frustration in their food seeking, territorial or sexual behaviour are often strikingly similar to that of man. Thus for the pragmatic approach of the investigator, there is no reason why he should not at least try to use animals for psychosomatic ('neuro-visceral') studies. As far as the second objection goes, it is of course, obvious that one has to choose an environmental situation like that which has been supposed to be psychogenic in humans. For this purpose we have now two methods at our disposal.

A first approach is furnished by an increasing number of observations that animals which have been rendered experimentally neurotic by the technique developed by Pavlov in dogs, and which has been applied successfully by MASSERMAN to cats and monkeys (MASSERMAN and PECHIEL, 1953) not only show neurotic behaviour patterns like apathy, or unexpected and inadequate flight or fight reactions, but also exhibit disturbances in the autonomic sphere such as food refusal, involuntary micturition or defaecation, vomiting, tachycardia, and disturbances of respiration, which like in the dog Nicky, described by GANTT (1944) are very similar to asthma. NOELPP and NOELPP (1951, 1952) have produced asthma-like attacks in guinea pigs by conditioning in a way very much resembling Dekker's experiments in humans (GROEN, 1958). Consequent application of these techniques might yield further interesting results.

Another approach is based on the observations of the ethologists, that frustrations occur regularly in the life of almost every animal living in its natural surroundings. In the case of animals living, like man, in social groups, these frustrations are most often caused by conflicts with other members of the group. The animals can react to these frustrations by outwardly directed neuromuscular behaviour like fight or flight; occasionally neurotic patterns seem to appear but we observe more often patterns of so-called displacement. Up till now the ethologists have been mostly interested in

the outwardly visible reaction patterns of their subjects, so that their studies of behaviour have been mostly restricted to the visible movements of the animal. However, as pointed out elsewhere (BARNET, 1958), if one defines ethology as the study of the behaviour of the organism as a whole, there is no reason to exclude changes in movement of smooth musculature, of heart and blood vessel function, or of glandular secretion from these studies. Thus it has been shown by BARNETT (1958) that if new wild rats are introduced into an established colony they are attacked by the most aggressive male member of the group and almost always die as a result. The interesting finding in this connexion was that the animal hardly ever dies from outwardly visible wounds, but from a state of exhaustion which may have its substrate in a depletion of the adrenal cortex of lipid material. We may also refer here to SCHUMK's (1954, 1955) work, which showed that in cats that were regularly exposed to barking dogs, without being able to flee or fight, an increase in blood pressure occurred leading to hypertrophy of the left ventricle. We have described elsewhere vomiting in female dogs as a result of conflicting emotions serving as a useful purpose for the feeding of the young (GROEN, 1955). Lately, we have observed abortion in pregnant hamsters that were kept with so many others in a small cage that there was no opportunity for them to build a nest. Thus, the study of naturally or experimentally induced frustrations in animals seems to offer an independent approach to the experimental study of psychosomatic disturbances.

OL.
5
0/61

SOCIOLOGICAL STUDIES

If we return to the concept that psychosomatic disturbances are exaggerations of what are in essence normal patterns, which all individuals exhibit in reaction to frustration in their interhuman contact, another independent method of approach becomes possible, viz. by the application of sociological studies. Modern sociology is largely based on the concept that the behaviour of individuals in groups is determined by laws which can be deduced from systematic observations. Social behaviour can be measured; it can be subjected to a test by predicting the behaviour of a group under certain circumstances. The most important research tool for the sociologist therefore is the statistical evaluation of measurable phenomena, observed in comparable groups. That psychosomatic medicine can derive benefit from the application of sociological methods is, amongst others, indicated by the fact that the prevalence of many of these disorders varies so markedly in different countries and even among different social groups within the same population. Thus ulcer of the stomach and duodenum was shown by KOUWENAAR (1938) in Indonesia to be fairly common among a group of Europeans and Chinese but to be practically absent in the Javanese. The prevalence of ulcer also differed markedly among workers in different branches of industry as found in Greater London (DOLL and AVERY JONES, 1951) and by VERTIN (1954) and his associates among the workers of the Philips factory in Holland. The possibility that nutritional or "constitutional" factors are responsible for these differences cannot be excluded. However, it is equally possible (and indeed this was admitted by the patients themselves), that the strains and stresses associated with their work situation may have contributed to the origin of the ulcers in one group more than in another. VON UEXKULL *et al.* have also drawn attention to certain interhuman factors in the etiology of peptic ulcer (PFLANZE *et al.*, 1956). We might

derive interesting knowledge if the sociologists could elucidate more about the exact nature of the pertinent strains and stresses.

Another example may be taken from a study of the psychogenic factors contributing to the causation of coronary thrombosis. Based on clinical observations and a number of biographies, we formulated a hypothesis which included the proposition that one of the precipitating events in this disease could be a marital conflict in which the patient felt disappointed and not understood by the spouse, who, instead of giving him the submissive love which he expected, confronted him with dominance, indifference, nagging or preference for others. In many cases this conflict was felt as a situation of love loss and frustation.

At first sight it seems as if such a purely psychiatric formulation does not lend itself to testing either by independent physiological or even by psychological methods. Nevertheless we deduced from this hypothesis the prediction that such a situation must have occurred significantly more frequently in the lives of divorced than of non-divorced married men, whereas it might also be anticipated that the love loss caused by the death of a marriage partner will be experienced in a similar way. We therefore predicted that if mortality and morbidity figures for coronary occlusion showed a higher incidence among divorced than among non-divorced married men, of the same age group, the hypothesis would be supported, thus using a sociological method, viz. biostatistics, to test a psychiatric hypothesis. Indeed it was found that in the American mortality statistics, there was a great excess in the mortality from coronary occlusion among divorced men, in whom, for all age groups there were more than one and a half times as many deaths as in the non-divorced married men; amongst widowers there was also a considerable excess (PERETZ and GROEN, 1959).

VOL.
5
1960/6

CONTROLLED THERAPEUTIC TRIALS

If the concept is correct that certain somatic disorders have a psychogenic etiology, it can be expected that methods of psychotherapy, if properly chosen and applied, must have a therapeutic effect in these conditions. Here again, is a fruitful testable prediction. Unfortunately, whereas the literature abounds with reports on the reputedly successful psychotherapy of patients with psychosomatic disorders, only very few of these relate to properly controlled studies.

A few examples may be given. GROEN and BASTIAANS (1951) GRACE, WOLF and WOLFF (1951) and PAULLEY (1956) have reported on the psychotherapeutic treatment of series of patients with ulcerative colitis. They had no control groups, so that they had to compare their results with figures taken from the literature on patients with ulcerative colitis treated by medical and surgical means. They concluded that the effect of psychotherapy was about the same as that claimed for medical and surgical treatment and suggested that this indicated that medical and surgical methods of treatment might work through their concomitant psychological influence. It is obvious that the lack of a comparable control group makes these conclusions tentative rather than conclusive.

ZETSEL (1944) compared the results in two groups of ulcer patients, one being treated by conventional methods of bed rest and diet, the other by group psychotherapy. The results were not worse and even somewhat better in the group treated with psychotherapy. Two investigations have recently been carried out on the effect of group therapy on bronchial asthma. SCLARE and CROCKET (1957) in

Glasgow reported no significant difference in improvement between the patients under group psychotherapy and those from a control group. However in GROEN and PELSER's (1959) therapeutic experiment a statistically significant difference between the treated and the control group was noted. As a last example a case of severe malignant hypertension may be quoted, described by GROEN *et al.* (1957). This patient improved to an extent of almost complete clinical cure after frontal leucotomy and psychotherapy. Although this observation concerns only one case, the fact that a patient who, according to all experience, should have been dead within 1 or 2 years, is healthy and at work 10 years after the operation, supports the hypothesis that the disease is of central nervous origin.

From these examples it will be clear how much still remains to be done in this direction. Up to the present the psychosomatic hypotheses have received relatively little support from the results of psychotherapy, not so much because psychotherapy has not been attempted in these cases, but because the psychotherapy was not planned for this purpose. It is hoped that those investigators who occupy themselves with the psychotherapy of psychosomatic disorders will realize that their work can serve a double purpose: the treatment or support of patients and the scientific testing of a theory.

SUMMARY

The writer, in discussing the methodology of psychosomatic research advocates the formulation of fruitful hypotheses which lend themselves to testing by independent validated methods. As such he reviews the contribution of psychiatric, psychological, physiological, experimental–biological and sociological methods of investigation and the evaluation of the results of properly controlled psychotherapeutic trials.

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VOL.
5
1960/6

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MENTAL AND PSYCHOSOMATIC MORBIDITY IN PEPTIC ULCER FAMILIES*

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PREDISPOSITION for mental or psychosomatic disease in peptic ulcer individuals has long since been a focus of interest in psychosomatic research. This interest was roused mainly by VON BERGMANN's (1913) theory that the imbalance of the vegetative nervous system of the ulcer individual was a manifestation of a "neuropathic" constitution. Several investigations have been made in order to elucidate this "neuropathic" constitution and assertain whether it might also manifest itself in some other way and thereby contribute to our knowledge of the nature of the personality of ulcer patients.

PREVIOUS INVESTIGATIONS

The literature in this field has recently been critically analyzed by GOSLING (1958). He stressed that many authors have reported a relatively low incidence of ulcer among psychotic patients but that the methods used had serious sources of error. Reports on the frequency of neurosis among ulcer patients vary from author to author.

The latest investigation is that reported by HØJER-PEDERSEN (1958). Comparing 51 male inpatients with duodenal ulcer and the same number of controls belonging to the hospital's personnel, he found a significantly higher frequency of neurotic features among the former (45 per cent as against 20 per cent of the controls). He likewise found alcoholism to be more common among the patients than among the controls (14 against 7). HØJER-PEDERSEN's series, however, might have been selected in some respects. For instance, about one fourth of the patients originally chosen had to be excluded because they had not been in hospital long enough to have been examined psychiatrically. Thus the series was to a certain extent selected as it consisted of patients who had been in hospital for a relatively long time. Since not all patients with ulcer were admitted to hospital, this might add to the possibility of a certain selection and thereby of a certain limitation of the value of the results. The composition of the control series might also be questioned. Of 82 persons, 21 had to be excluded because of dyspepsia, and 6 because they refused to co-operate. The description of these 6 persons suggests that their refusal might have been due to neurosis.

In a previous investigation (WRETMARK 1953) the author studied the distribution of ulcer among different psychiatric diagnostic groups compared with a control material selected from the same psychiatric clinic. Among the persons who had had duodenal ulcer the frequency of asthenic insufficiency was found to be relatively high. Anxiety and vegetative lability were often the dominating symptoms. An equally marked difference was found for the frequency of endogenous depression. This diagnosis was noted 3 times as often among the controls as among the duodenal ulcer individuals. In contrast, neurotic depression was over-represented among those who had had duodenal ulcer.

GOSLING (1958) has since made a similar investigation on a psychiatric series from the Bethlem Royal and Maudsley Hospitals. In comparison with a normal population he found peptic ulcer to be less common among schizophrenics and more common among neurotics, particularly among those of depressive nature. Among manic-depressive patients the observed frequency did not differ from that expected. Only on comparison of the frequency of ulcer among manic-depressive patients with that in the entire psychiatric series were the frequencies lower than expected. Moreover GOSLING

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found a higher frequency among those who had been admitted because of alcoholism and among those who also suffered from asthma. GOSLING's observation that ulcer is common among alcoholics is in line with the results of previous investigations by ENGESET (1956) and HAGNELL and WRETMARK (1957).

Of the modern literature on the problems under discussion mention might be made of the monograph by HØJER-PEDERSEN (1958), which also contained an investigation of the predisposition for mental disease in ulcer individuals compared with controls. He concluded that this predisposition is, generally speaking, "undoubtedly much more pronounced among ulcer patients". The figures given by HØJER-PEDERSEN do not, however, prove this statement. He reported only a certain preponderance of "neuroses" respectively "alcohol addiction" in the families of patients with ulcer. This preponderance was not statistically significant. The value of the results is limited still more by the fact that he does not describe what is to be understood by the term "family".

To summarise, available investigations of the predisposition of ulcer individuals to psychic or psychosomatic disease have not provided a satisfactory or unequivocal answer to the questions posed.

The purpose of the present investigation was to determine the morbidity among close relatives of ulcer patients and so, if possible, to reveal any predispositions in such relatives as compared with those in a normal population.

SERIES

The series and the principles by which the subjects were selected have been described previously (WRETMARK, 1953). As only duodenal ulcer is dealt with here, the series consisted of 130 male inhabitants in a medium sized Swedish town, admitted to the medical department (Örebro) with this diagnosis during the years 1935–41. At the time of the investigation (1949–51) none of the patients were above 70 years. For a patient to be accepted X-ray examination must have shown a niche, or the patient must have had a typical history together with constant typical deformation of the bulb. The 130 individuals represented 93·8 per cent of those who had been requested to present themselves for examination.

The controls were selected from the district register, the first male inhabitant born after each proband in Örebro being taken as a control, provided that he had not had peptic ulcer. Of the controls, 94·9 per cent were examined.

The ulcer series also included 34 patients with gastric ulcer, 2 with both duodenal and gastric ulcer, and one in whom the site of the ulcer could not be determined. Controls were also selected in the same way for these patients. The entire control material consisting of 169 persons is used for comparison. The mean age of the control series (44·7 years) is only slightly higher than that of the duodenal ulcer series (44·0 years), which can hardly impair the comparability of the series.

METHOD

On the basis of a minor pilot study a questionnaire was drafted including about 150 standard questions. These questions were put to all persons in the course of an interview lasting 2–3 hr. The interviews had the character of a conversation during which the questions were asked in the order best suited to the situation. If the contact achieved on the first occasion was not satisfactory or if the interview tended to be too long the interview was repeated.

In 38 cases in which the information appeared scanty or unreliable, supplementary data were obtained from close relatives. Information on mental disease, if any, among the parents and siblings was checked as far as possible by examination of hospital records.

VOL.
5
1960/6

The data to be analyzed were thus obtained not from personal interviews with relatives but mainly on reports by the probands and their controls.

There might be some differences in the opinions between the two groups on the mental state of health of family members just as there might be a difference in their motivation to report or to conceal the occurrence of mental diseases. In view of the now widely accepted opinion that ulcer has something to do with neuroticism and mental conflicts it is possible that patients with ulcer are more interested in the mental state of members of the family and therefore have better knowledge of it than others. The more distant the relatives the greater the above-mentioned source of error will tend to be. However, all of the persons included in the investigation were systematically questioned in an identical manner about the health of their relatives. Questions were asked not concerning groups of relatives as a whole, but regarding each relative separately.

The method implies that the morbidity figures found must be regarded as minimal values.

The statistical analysis could be kept simple because it was found that the ulcer families did not differ in size from the control-families (7·45 : 7·22 members) and that the sex distribution was also similar in both series. As to the age distribution, there is strong reason to believe that this was also the same. The ulcer patients and the controls were, practically speaking, of equal age. Nor did they differ regarding their position among the siblings. Neither the probands nor the controls therefore showed any tendency to belong to the oldest or youngest of the siblings. The number of siblings who had died was the same in the families compared. Differences in age at death can hardly play any role because only those siblings were accepted who were alive at the time the series was collected.

In the statistical analysis the following formula was used for determination of the sigma values (z).

$$z = \frac{p_1 - p_2}{\sqrt{p_T\,(100 - p_T)\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}}$$

In the formula p = percentage, p_T = percentage in both series combined and n the number of individuals in each series.

Unless otherwise stated, the significance was tested by the two-tailed test because there was, as a rule, no reason to expect differences in any definite direction.

RESULTS

Mental morbidity

If the term family is to be understood as covering all relatives known to the proband, 101 ulcer individuals (78·9 per cent) and 97 controls (54·7 per cent) stated that one or more relatives had had some mental disease. As mentioned above, such a calculation has serious inherent sources of error.

The comparison is more reliable if the families be limited to those members of whom the probands possessed most knowledge, i.e. parents and siblings. The mental morbidity among these is given in Tables 1 and 2. In these tables all fathers, mothers and siblings who had children respectively siblings with ulcer are classified as "father of ulcer individual", "mother of ulcer individual", etc. Twenty one fathers and 21

mothers of the controls had some other child with ulcer and were consequently transferred to the ulcer group. Eighty brothers and 62 sisters were similarly transferred because they had a sibling with ulcer. In this way families with ulcer in one or more members were compared with families without ulcer. It might be mentioned that these manipulations had no effect on the age distribution in the groups compared.

The figures in the tables refer to individuals. Thus, for example, an alcoholic with neurotic symptoms appears in the table only as an alcoholic. Therefore the frequency

TABLE 1.—MENTAL MORBIDITY AMONG PARENTS OF ULCER INDIVIDUALS AND OF CONTROLS

	Fathers of				Mothers of			
	Ulcer individuals ($N = 155$)		Controls ($N = 127$)		Ulcer individuals ($N = 153$)		Controls ($N = 120$)	
	n	Per cent	*n*	Per cent	*n*	Per cent	*n*	Per cent
Alcoholism	28	18·0	11	8·7*	0	0·0	1	0·8
Schizophrenia	0	0·0	0	0·0	2	1·3	3	2·5
Manic-depressive reaction	1	0·6	1	0·8	2	1·3	3	2·5
Epilepsy	0	0·0	0	0·0	1	0·6	1	0·8
Neurosis	9	5·8	0	0·0†	16	10·4	5	4·2‡
Organic nervous disease	0	0·0	1	0·8	0	0·0	1	0·8

* $0{\cdot}02 < P < 0{\cdot}03$
† $0{\cdot}001 < P < 0{\cdot}01$
‡ $0{\cdot}04 < P < 0{\cdot}05$

TABLE 2.—MENTAL MORBIDITY AMONG SIBLINGS OF ULCER INDIVIDUALS AND OF CONTROLS

	Brothers of				Sisters of			
	Ulcer individuals ($N = 329$)		Controls ($N = 260$)		Ulcer individuals ($N = 394$)		Controls ($N = 296$)	
	n	Per cent	*n*	Per cent	*n*	Per cent	*n*	Per cent
Alcoholism	11	3·3	6	2·3	0	0·0	0	0·0
Schizophrenia	1	0·3	2	0·8	1	0·2	1	0·3
Manic-depressive reaction	0	0·0	3	1·1	3	0·7	2	0·7
Epilepsy	2	0·6	1	0·4	1	0·2	2	0·7
Neurosis	10	3·0	9	3·5	25	6·3	15	5·1
Organic nervous disease	3	0·9	2	0·8	2	0·5	2	0·7

of neurosis given in the tables is somewhat too low, but not so low as to be of any significance.

It is clear from Table 2 that the figures given there do not support the assertion of DRAPER and TOURAINE (1932) that boys are more common than girls in ulcer families. KELLOCK (1951) found, if anything, a preponderance of females in his series.

The frequency of alcoholism was somewhat higher among fathers of ulcer individuals. Whether it was a question of real alcoholism (chronic alcoholism, addiction)

VOL. 5 1960/6

in all cases cannot, of course, be decided with certainty. However, there is hardly any doubt that the abuse of alcohol was fairly severe and that it had placed a severe strain on the family. The fathers in these cases were very often described as incalculable and continuously threatening the harmony and feeling of security of family life.

For comparison it might be mentioned that ESSEN–MÖLLER (1956) found the frequency of alcoholism to be 9·2 per cent among the male population above 14 years in a Swedish rural district. The highest frequency was in the 50–59 year age group, in which it was 16·4 per cent . Thus, the figures given in Table 1 agree fairly well with those found by other authors on the basis of personal interviews.

The difference in the frequency of alcoholism between fathers of ulcer patients and fathers of controls, as given in Table 1, is statistically probable but not significant ($0{\cdot}02 < P < 0{\cdot}03$). The difference shows the same tendency as that reported by HØJER–PEDERSEN (1958).

In this connection it might be mentioned that peptic ulcer has regularly been found to be more common among alcoholics than in the normal population (ENGESET 1956; HAGNELL and WRETMARK 1957; GOSLING 1958). On the other hand, the percentage of alcoholics among ulcer patients does not appear to be high. This holds whether ulcer series from psychiatric clinics be compared with non-ulcer members from the same population (WRETMARK 1953), or whether ordinary ulcer patients be compared with a random selection of persons without gastric trouble (HAGNELL and WRETMARK 1957). These investigations thus do not verify the very high frequency of alcoholics reported by KAPP, ROSENBAUM and ROMANO (1947) in a small ulcer series.

Table 1 also shows a higher frequency of "neurosis" among fathers and mothers of individuals with ulcer than among parents of the controls. The word neurosis is to be understood here as a group name for all obvious nervous disturbances of more chronic nature but without psychotic features. Neither did it include simple asthenic conditions. As to the fathers, the difference was significant ($0{\cdot}001 < P < 0{\cdot}01$); for the mothers it was statistically probable ($0{\cdot}04 < P < 0{\cdot}05$). The differences show the same tendency as those found by HØJER–PEDERSËN for entire families. It is of some interest that only 4 of the 26 mothers of ulcer individuals who were married to alcoholics were classified as suffering from neurosis.

Comparison of the total mental morbidity among relatives of ulcer individuals compared with that in relatives of the controls revealed that, of 1031 close relatives of the ulcer individuals (parents and siblings), 127 (12·3 per cent) were described as havong some mental disease. Of 803 persons belonging to the control families 75 (9·3 per cent) were described as having some silimar disorder. This difference is statistically probable ($0{\cdot}02 < P < 0{\cdot}04$).

Because of the sources of error described previously, it is difficult to assess the reliability of these figures. Some idea of their reliability might be gained by comparing them with data found in population studies in which all the individuals were interviewed personally. A comparison between the frequencies found in the control ulcer families as a whole, and those given by ESSEN–MÖLLER (1956) and FREMMING (1947) is given in Table 3. Apart from neurosis the table includes only such clinical entities as could be said to be fairly well defined.

It is clear from Table 3 that a surprisingly good agreement was found between the frequencies based on data anamnestically obtained from probands and controls and the frequencies based on census investigations. Thus this suggests that the figures found are fairly reliable. This conclusion can not, however, be strictly applied to

such less well defined entities as alcoholism, neurosis or abnormal personality. It is therefore not certain what importance should be attached to the statistically probable preponderance of "neurosis" among relatives of patients with ulcer.

Of the fathers with ulcer and mental lability (alcoholism, neurosis), 43·9 per cent of the sons had ulcer. The corresponding figure for fathers with ulcer but without such mental lability was 39·5 per cent. The percentages are calculated on the total number of sons, the probands included. Thus fathers with ulcer have the same tendency to produce sons with ulcer, whether they are mentally disturbed or not.

TABLE 3.—FREQUENCIES GIVEN BY VARIOUS AUTHORS FOR SCHIZOPHRENIA, MANIC-DEPRESSIVE REACTION, EPILEPSY AND NEUROSIS

	Ulcer family ($N = 1031$) WRETMARK	Control family ($N = 803$) WRETMARK	Normal population ($N = 2550$) ESSEN-MÖLLER	Normal population ($N = 2756$) FREMMING
	Per cent	Per cent	Per cent	Per cent
Schizophrenia	0·4	0·7	0·9	0·9
Manic-depr. reaction	0·6	1·1	0·5	1·6
Epilepsy	0·4	0·5	0·6	0·3
Neurosis	5·8	3·6*	7·0	2·2

* $0{\cdot}02 < P < 0{\cdot}03$

The higher percentage of schizophrenia and manic-depressive psychosis among the control families did not differ significantly from that found in the ulcer families. Several authors have previously reported a low frequency of ulcer among patients with psychosis. It has, however, been pointed out that such social categories known to have a higher frequency of ulcer, e.g. foremen, are under-represented among schizophrenics. The low frequency might also be related to institutionalization. Both of these arguments have been met by GOSLING (1958). His material included 399 schizophrenic males who could not be characterized as institutionalized, and among these he observed 4 who had had ulcer, as against 12·2 expected. The low frequency with which ulcer was found in psychotics in general could be ascribed almost entirely to the low frequency among schizophrenics. On the basis of his findings GOSLING concludes: "If it is assumed that the incidence of peptic ulcer is an index of the organisms vulnerability to environmental stress, then, in general, there is at the one extreme the withdrawn schizophrenic and the other the over-reactive neurotic; the former is relative immune to ulcer and the latter is abnormally prone," Although the figures found in the present investigation do not support GOSLING's conclusion, neither do they argue against it.

Despite limitations due to the lack of statistical significance the relatively low frequency of endogenous depression found in the peptic ulcer families is in line with the authors (1953) previous finding that ulcer individuals are under-represented among patients with this diagnosis in a psychiatric clinic. It is also in line with GOSLING's (1958) finding mentioned above that ulcer was less common among manic-depressives than in a mixed psychiatric series. It also agrees with the assumption that manic-depressive reactions and ulcer show a predilection for individuals of different body-build and that most experimental observations suggest that depression is associated with gastric hypofunctioning.

VOL.
5
1960/6

Of those who have studied the occurrence of ulcer in psychotics Ross, HAY and MCDOWALL (1950) reported a frequency of only 0·6 per cent of 1608 patients in a Canadian mental hospital. This low figure, which is most probably lower than that in a normal population, might also be considered in the light of the fact that manic patients had a relatively high frequency of ulcer. The results cannot, however, be regarded as reliable because no correction was made for age and sex. In addition, on X-ray investigation of the gastro-intestinal tract, HENRY (1931) found gastric hyperfunction in manic conditions but not in depressive states. Investigations of manic and depressive conditions in general appear to indicate that these states represent opposite extremes of the functional state of the vegetative system. Recently BERGSMAN (1959) found this difference to be reflected in a high excretion of adrenalin in the urine in manic conditions, in contrast to a low excretion in depressive states.

On close examination of 48 patients with duodenal ulcer admitted to the psychiatric department, HØJER–PEDERSËN (1959) found no case of endogenous depression. On the other hand, all could be classified as dysphoric neuroses frequently complicated by alcohol addiction.

In view of the results of previous statistical investigations on hospital series in combination with the experimental observations, it might be concluded that there are at least relatively strong reasons to expect a difference in the frequency of manic-depressive disease (endogenous depression) between the families in the direction indicated in Table 3. This would then allow of the statistical significance being tested by the one-tailed test, which shows a tendency in the statistical meaning of the word ($0{\cdot}05 < P < 0{\cdot}10$).

Psychosomatic Morbidity

In psychosomatic research and theorizing the specificity problem has occupied a prominent position. Some authors claim that the "choice of organ" is related to a psychophysiologic regression, which is determined mainly by the particular structure of an emotional conflict. Others attach more importance to the nature of the inherited predispositions or claim that every individual has his special "reaction organ" varying with the individual development of the personality and that this organ is always or mainly activated in association with any sort of stress. The specificity problem might be elucidated by investigation of the distribution of various psychosomatic diseases in the population, and determining, for example, whether the clinical picture of a given individual varies with the environmental conditions under which it developed.

Since the data on the morbidity in the families obtained from ulcer individuals and controls appeared to be reliable, it might also be used in studying the occurrence of psycho-somatic disease. The predilection for such disease in the families concerned may represent one aspect of the specificity problem.

Previous investigations have shown that ulcer is more common in relatives of ulcer patients than in a normal population (DOLL and BUCH 1950; WRETMARK 1953). The frequencies of some other diseases which might more or less be regarded as psychosomatic are given in Table 4 and 5.

It is clear from the tables that the fathers and sisters of ulcer patients had gastritis more frequently than corresponding members of the control families. The differences were significant. As to the mothers and brothers, the same tendency was observed, but the difference was not statistically significant. Here gastritis is to be understood as reported symptoms of gastritis, or symptoms of ulcer character, although ulcer had not been diagnosed. Occasional or transient symptoms of dysfunction of other parts of the digestive tract were ignored.

Otherwise no differences were found. GOSLING's (1958) observation that ulcer was more common than expected among asthmatics is not reflected in the figures. If asthma be isolated from the group allergic diseases (here including asthma, urticaria, hay-fever) and the calculation be based on the entire family, there will be 18 (1·7 per cent) asthmatics among 1031 relatives of ulcer individuals as against 8 (1·0 per cent) of 803 relatives of controls. The difference is too small to be regarded as a tendency. Owing

TABLE 4.—PSYCHOSOMATIC MORBIDITY AMONG PARENTS OF ULCER INDIVIDUALS AND CONTROLS

	Fathers of				Mothers of			
	Ulcer individuals ($N = 155$)		Controls ($N = 127$)		Ulcer individuals ($N = 153$)		Controls ($N = 120$)	
	n	Per cent	*n*	Per cent	*n*	Per cent	*n*	Per cent
Gastritis	21	13·5	5	3·9*	11	7·2	7	5·8
"Allergic" disease	6	3·9	1	0·8	4	2·6	5	4·2
Migraine	0	0·0	0	0·0	4	2·6	4	3·3
Hypertension	11	7·1	7	5·5	21	13·7	18	15·0
Biliary disease	2	1·3	2	1·6	16	10·4	12	10·0
Thyrotoxicosis	0	0·0	1	0·8	8	5·2	2	1·7

* $0{\cdot}001 < P < 0{\cdot}01$

TABLE 5.—PSYCHOSOMATIC MORBIDITY AMONG SIBLINGS OF ULCER INDIVIDUALS AND CONTROLS

	Brothers of				Sisters of			
	Ulcer individuals ($N = 329$)		Controls ($N = 260$)		Ulcer individuals ($N = 394$)		Controls ($N = 296$)	
	n	Per cent	*n*	Per cent	*n*	Per cent	*n*	Per cent
Gastritis	28	8·5	12	4·6	24	6·1	6	2·0*
"Allergic" disease	9	2·7	5	1·9	10	2·5	4	1·3
Migraine	1	0·3	2	0·8	2	0·5	5	1·7
Hypertension	5	1·5	4	1·5	20	5·1	11	3·7
Biliary disease	1	0·3	3	1·1	18	4·6	6	2·0
Thyrotoxicosis	2	0·6	3	1·1	12	3·0	17	5·7

* $0{\cdot}001 < P < 0{\cdot}01$

to the method used the values found refer largely only to allergic manifestations in adulthood.

Nor do the tables substantiate the observation of WRETMARK (1953) that arterial hypertension was more common among controls than among ulcer patients. DRAPER and TOURAINE's (1932) claim that ulcer patients and patients with cholecystopathy represent somatological counter-poles could not be confirmed in the families. This also applies to the connection, suggested by some authors, between thyrotoxicosis and peptic ulcer.

VOL. 5 1960/6

Comparisons are also possible between the frequency of psychosomatic diseases in ESSEN-MÖLLER's census investigation. Such a comparison is given in Table 6.

The figures are not strictly comparable. The table is given to show that despite the different methods used the values obtained were of roughly the same order, which again supports the assumption that probands and controls were fairly well informed about the state of health of the family members.

The families of the ulcer individuals and controls, however, represent a selection of adults and older persons, while ESSEN-MÖLLER's figures refer to an entire population.

TABLE 6.–PSYCHOSOMATIC MORBIDITY IN THE DIFFERENT SERIES COMPARED WITH DATA FROM ESSEN-MÖLLER'S CENSUS INVESTIGATION

Disease	Females						Males					
	Ulcer family ($N = 547$)		Control family ($N = 416$)		ESSEN-MÖLLER's data ($N = 1238$)		Ulcer family ($N = 484$)		Control family ($N = 387$)		ESSEN-MÖLLER's data ($N = 1312$)	
	n	Per cent	*n*	Per cent	*n*	Per cent	*n*	Per cent	*n*	Per cent	*n*	Per cent
Gastritis	35	6·4	13	3·1	103	8·3*	49	10·1	17	4·4	87	6·7*
Asthma	10	1·8	6	1·4	20	1·6	8	1·6	3	0·8	33	2·5
Migraine	6	1·1	9	2·2	60	4·8	1	0·2	2	0·5	21	2·8
Hypertension	41	7·5	29	7·0	160	12·9†	16	3·3	11	2·8	101	7·7†
Biliary disease	34	6·2	18	4·3	46	3·8	3	0·6	5	1·3	9	0·7
Thyrotoxicosis	20	3·7	19	4·6	16	1·3	2	0·4	4	1·0	1	0·1

* The figures refer to "mixed digestive complaints" (ulcer and biliary disease excluded).
† Coronary diseases and myocarditis included.

This might explain the differences in the frequency of biliary disease. As to thyrotoxicosis, it is well known that the frequency of goitre of more or less toxic nature differs from one part of the country to another. The higher frequency of migraine in ESSEN–MÖLLER's material, on the other hand, is difficult to explain.

DISCUSSION

The results presented give the impression that the method used gave frequencies which were comparable to those obtained in census investigations. They did not suggest that ulcer individuals are more willing than controls to report, or are more familiar with, the occurrence of mental or psycho-somatic disease in other members of the family. This suggests that the differences found between relatives of ulcer patients and relatives of controls might be regarded as true differences.

The excessive incidence of alcoholism among fathers, and "neurosis" among fathers and possibly also among mothers, are in conformity with the results of some earlier investigations which have been referred to previously. It might also be mentioned that DOWNES (1942, 1953), provided evidence that psychoneurosis in one member of a family is associated with a higher incidence of disease in the other family members. BUCK and LAUGHTON (1959) trying to pursue this observation, found that all types of illness were more common among children of psychoneurotic mothers. When correction was attempted for such artefacts as psychoneurotic mothers being more apt to seek medical care for their children, the only certain excess was that of behavioural and psychosomatic disorders.

The frequency of alcoholism among brothers of ulcer patients as well as of the controls was strikingly low in contrast to the frequency reported for fathers of controls, which corresponded roughly to that expected. Of the entire male population over 15 years, ESSEN–MÖLLER found that 4 per cent were registered with a temperance board,

which thus means a somewhat higher figure than that found for the brothers. Since it is known that the number of alcoholics registered is always lower than the true number, it is probable that the brothers of alcoholics in the two series had concealed or minimised existing alcoholism.

SUMMARY AND CONCLUSIONS

The purpose of the present investigation was to elucidate the predisposition to mental or psychosomatic disorder in peptic ulcer individuals. The morbidity in families in which duodenal ulcer had occurred was compared with that in ulcer-free control families.

It was found that fathers of ulcer patients were more frequently described as being addicted to alcohol. The difference was statistically probable ($0{\cdot}02 < P < 0{\cdot}03$). In addition in ulcer families the fathers were more frequently neurotic ($0{\cdot}001 < P < 0{\cdot}01$). The mothers were probably more frequently neurotic ($0{\cdot}04 < P < 0{\cdot}05$). The siblings of ulcer patients did not appear to be unusually mentally disturbed. The high frequency of ulcer was found to be the single common factor to the parents and the children. It therefore appears that the disposition to react with ulcer is transmitted with a high degree of specificity.

Children of mentally disturbed fathers with ulcer did not appear to be more prone to ulcer than children of mentally normal fathers with ulcer.

The frequently reported negative correlation between peptic ulcer and psychosis was not reflected with certainty by a lower frequency of psychosis in the ulcer families. A tendency in this direction, however, showed that this point deserves further attention.

Investigation of the occurrence of a number of other diseases generally regarded as psycho-somatic suggested that only gastritis was over-represented in relatives of ulcer patients. Judging from the results, there was thus no general tendency to react with dysfunction or disease of some organ or organ-system other than the gastro-duodenal tract. This also suggests that the familiar disposition to ulcer should be regarded as specific.

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AN ENDOCRINE STUDY OF DEPRESSIVE ILLNESS*

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THERE are few reports in the literature of serial studies of thyroid and adrenocortical activity throughout the course of depressive illness. Attention has in the main been directed to the effects of short-lived emotional stress and physical procedures such as electro-convulsive therapy (E.C.T.) on the activity of the two glands. (HETZEL *et al.*, 1952; BLISS *et al.*, 1956; BOARD *et al.*, 1957).

The study that is reported here has extended over several years in an attempt to explore the gap in our knowledge of the natural history of affective disorder from the point of view of thyroid and adrenocortical activity. Control studies, however desirable, have been impracticable, as they would have necessitated normal subjects submitting themselves to a rigid discipline for periods of several weeks.

MATERIAL AND METHODS

The material consists of clinical and biochemical observations throughout 21 depressive illnesses in 17 patients, 2 patients being admitted twice, and 1 patient three times during the study. As a result 19 serial studies of steroid excretion were made. The steroid estimations were made on successive 24 or 48 hr collections, except for a few early cases in which estimations were made three times a week. Completeness of collection was assessed by carefull ward observation, and by the creatinine content. Collections were on the whole very satisfactory, so that the figure quoted are the actual values estimated, and no correction for creatinine content has been made. Occasional incomplete collections were discarded, and in some patient series occasional days were missing, because of unavoidable circumstances such as the patient going out for the weekend.

Thyroid function was assessed by the estimation of the serum protein bound iodine made at weekly intervals. Thirteen such patient series were collected. Initial protein bound iodine estimations were made during the first week after admission on a further 5 patients, and on 9 patients the neck–thigh ratio of ^{132}I activity was also measured.

THE PATIENTS

The subjects for this study were all male patients who had been admitted to the Metabolic Ward of the Maudsley Hospital and in whom depression was the predominant disorder. In each case the illness was severe enough to make normal life impossible, and several patients had attempted suicide. Most patients had lost a little weight as a result of poor appetite, put none was severely malnourished. The periods of observation varied from 5 to 12 weeks (mean: 8 weeks).

The mean age on first admission was 45·7 years (range 23–57 years). The duration of illness, or at least of major symptoms, before admission varied from 10 days to 6 months (mean: 3 months). On three occasions recovery occurred without physical treatment (Nos. 3, 10 and 17). The other 18 episodes were treated with electro-convulsive therapy (E.C.T.); one patient failed to respond (No 2), another responded well

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VOL. 5 1960/61

but promptly relapsed (No. 21), and 3 patients recovered only very slowly (Nos. 6, 8 and 16). In the remaining 13 instances depression was rapidly relieved, although minor symptoms sometimes persisted a little longer.

METHODS

The following methods have been used:

(1) Urinary creatinine by the method of Folin.

(2) Urinary total neutral 17-ketosteroids (17KS) by a slight modification of the method recommended by the Medical Research Council Committee on Clinical Endocrinology (1951). The normal range in relation to age is taken from HAMBURGER (1948). The S.D. of the differences in a series of 34 urines each estimated in this laboratory on two separate occasions was 0·68 mg per 24 hr.

(3) Urinary acid stable formaldehydogenic substances (ASFS), a measure of gluco-corticoid excretion, by the method of TOMPSETT (1953) and TOMPSETT and SMITH (1954). The normal range in this laboratory is 3–11 mg per 24 hr. The S.D. of the differences in a series of 26 urines each estimated on two separate occasions was 0·77 mg per 24 hr. The use and significance of these methods in serial studies has been described previously (WILLCOX, 1959).

(4) The serum protein bound iodine (PBI) by a slight modification of the method of GROSSMAN and GROSSMAN (1955). Normal range 3·3–7·4 μg per 100 ml. The S.D. of the differences in a series of 44 sera, each estimated on two separate occasions, was 0·44 μg per 100 ml.

(5) The neck—thigh ratio of ^{132}I activity by the method of HALNAN (1958) using an exact copy of the apparatus described.

TABLE 1.—WEEKLY ESTIMATIONS OF SERUM PROTEIN BOUND IODINE DURING DEPRESSIVE ILLNESSES

No	PBI μg per 100 ml												Mean
2	5·9	6·2			5·8	5·9	4·9	5·7	4·9				5·7
3	4·4	4·0		4·2	4·3	4·3							4·2
4	4·7		5·2	4·8	4·3	5·1	5·0	4·7	5·1	5·3	5·4	5·5	5·0
5	4·8												4·8
7	6·5	6·0	5·4	4·1	5·1	4·8			5·1				5·3
8	6·5	6·9	7·1	7·4	7·8	6·8	6·8	6·0	7·3	7·2			6·9
9	5·9	5·6	5·3	5·9	4·9								5·5
10	5·6	5·7	5·4	4·8	4·1	4·9	5·0						5·1
11	3·9	4·2	3·7	3·3	3·9								3·8
12	4·0		3·9	4·7	4·6								4·3
13	5·3	5·3	5·0	4·7	5·2	5·4	5·4	4·7	4·3	4·7			5·0
14	6·2	5·2	4·2	3·8	3·9	3·1	4·7	4·4	5·3	3·4	3·7	3·3	4·3
15	5·0	4·4	4·0	3·1	3·8	4·0	4·5						4·1
16	4·3	3·8		3·8	3·6	4·0	3·1	3·9	2·9	3·1			3·6
17	3·8												3·8
18	5·0												5·0
19	5·1												5·1
20	5·6												5·6
	Group Mean:												4·8

RESULTS

The main findings are summarised in Tables 1 and 2 for thyroid function and adrenocortical function, respectively. In addition, the neck—thigh ratio of ^{132}I activity was estimated for 9 patients before any improvement had occurred. These values were all within the normal range, and gave a mean of 3·7 compared with a mean of 3·9 for 10 euthyroid subjects.

TABLE 2.—RANGE OF EXCRETION OF 17KS AND ASFS DURING DEPRESSIVE ILLNESSES

		17KS			ASFS	
No	Age	Normal range for age	Observed range	Mean	Observed range	Mean
1	35	7–24	7–20	(14·2)	5–15	(8·7)
2	54	4–17	6–25	(16·3)	2–17	(9·5)
3	47	5–19	3–27	(13·4)	5–15	(8·3)
4	22	7–23	15–35	(22·4)	2–15	(8·4)
5	52	4–17	14–32	(23·5)	4–15	(9·0)
6	53	4–17	5–22	(16·2)	8–18	(12·0)
7	56	3–15	5–14	(7·9)	5–18	(7·8)
8	32	8–25	8–22	(17·0)	2–19	(10·1)
9	44	6–20	9–18	(14·0)	4–11	(7·9)
12	32	8–25	10–22	(15·6)	2–18	(9·3)
13	52	4–17	14–26	(18·2)	4–10	(7·6)
14	53	4–17	5–13	(9·6)	2–12	(7·4)
15	55	4–16	5–9	(7·1)	5–15	(9·5)
16	32	8–25	11–20	(15·4)	6–12	(8·8)
17	57	3–15	8–12	(9·9)	4–9	(6·8)
18	40	6–22	10–27	(15·1)	6–25	(13·5)
19	53	4–17	14–27	(21·8)	6–21	(10·6)
20	23	7–23	12–27	(20·6)	7–17	(12·1)
21	47	5–19	8–14	(12·6)	8–20	(10·1)

All values in mg per 24 hr.

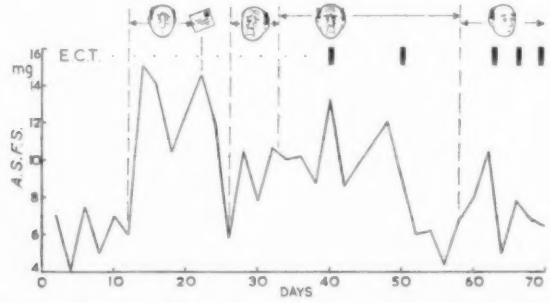

FIG. 1.—ASFS excretion in patient No. 5. This patient was flown to this country following a suicidal attempt, leaving his wife abroad. Depressed on admission, after 10 days he became anxious and worried by the absence of letters from his wife. Relieved temporarily by the receipt of letters, his depression persisted and anxiety soon increased again. There was a good response to E.C.T., which the patient was at first unwilling to receive.

Findings from individual patients are illustrated in Figs 1–5.

DISCUSSION

Although there are a few values slightly beyond the accepted normal limits of serum PBI for the method used, the means for all patients with serial observations are well within this range, and the mean for the whole group (4·8) compares closely with the normal mean (5·0 μg). Variation in individual series was small, being seldom much in excess of 1 μg (cf. ENGSTROM and MARKARDT, 1954; MARGOLESE and

VOL. 5 1960/61

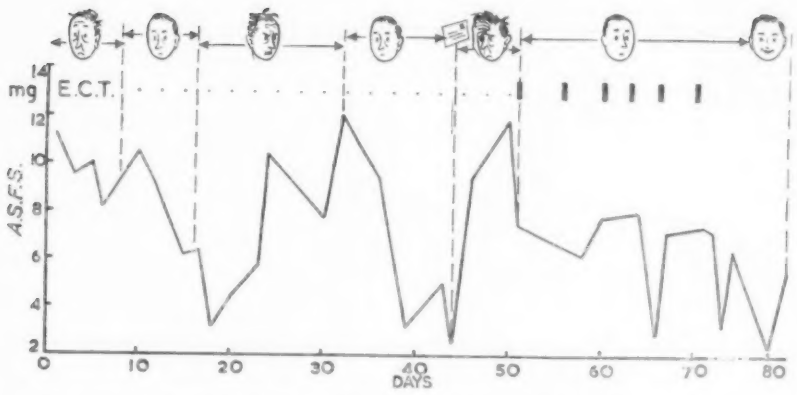

FIG. 2.—ASFS excretion in patient No. 14. The illness ran a fluctuating course for the first 6 weeks following admission. The patient then relapsed for the second time having been upset by a letter from his office chief. Failure to obtain expected promotion had appeared to be a precipitating factor in this illness. Steady improvement followed the starting of a course of E.C.T.

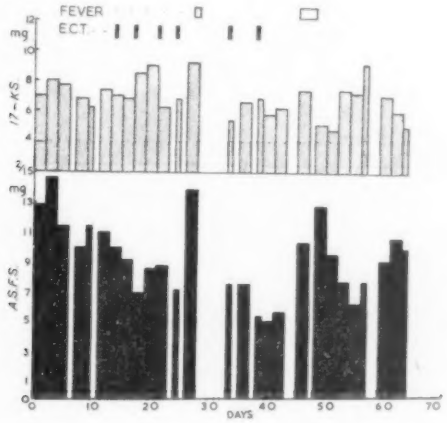

FIG. 3.—ASFS and 17KS excretion in patient No. 15. Depressed and anxious on admission this patient improved with the start of E.C.T. His apparently steady progress was twice interrupted by brief bouts of pyrexia due to recurrent chronic bronchitis. Worry over repeated absences from work due to these attacks had been a factor in the development of his depression. He became anxious during these brief pyrexial periods. His ASFS excretion rose sharply, and can be attributed to both anxiety and pyrexia. Excretion values of the same order attributable to anxiety only are seen on admission. The 17KS excretion is also shown. There are minor fluctuations. This patient was free from sexual problems.

GOLUB, 1957). In 2 patients there was variation in excess of 2 μg. This was mainly due to a steady decrease in level during the first few weeks. Both these patients were anxious as well as depressed on admission, and improved during this period. Subsequent fluctuations occurred in patient No. 14, and the changes in serum PBI throughout paralleled those in the ASFS excretion. This is a correlation noted previously in some patients (GIBSON and WILLCOX, 1957).

Comparison of the mean values for the first and last estimations of serum PBI

show a small difference which is statistically significant (mean difference $-0{\cdot}52\ \mu g$; $t = 2{\cdot}371 : 0{\cdot}05 > P > 0{\cdot}02$), but it is doubtful whether the changes in individual patients are of clinical significance, except in the two cases referred to above.

In contrast to the minor changes found in thyroid function, variation in adrenocortical function as assessed by the 17KS and ASFS measurements was considerable.

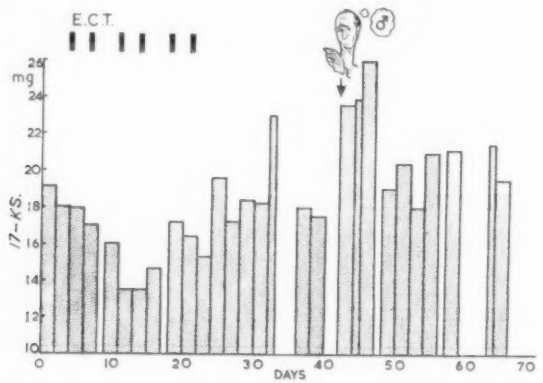

FIG. 4.—17KS excretion in patient No. 13. There are minor fluctuations around the upper limit of normal for his age. For a period of 5 days following the receipt of a letter from his wife relating to sexual difficulties the 17KS excretion rose sharply and remained at levels beyond the normal for his age. The patient was very disturbed by this letter.

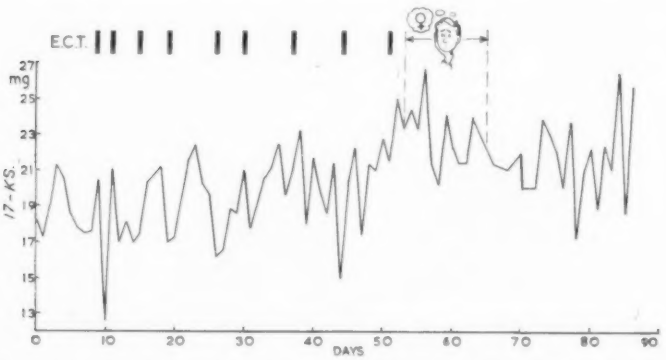

FIG. 5.—17KS excretion in patient 20. Masturbation guilt, feelings of guilt and inadequacy related to failure in a first attempt at sexual intercourse, a belief that he was "oversexed" and indecision regarding the prospect of a formal engagement were recurring features of this patient's mental content. During the period indicated he had "now become almost totally preoccupied with sexual problems."

Thus, in 8 of the series for which data are given in Table 2, there are numerous 17KS values in excess of the normal range for the age of the patients concerned, and high values of ASFS excretion were present in 16 series out of the 19. When the data of each patient are examined graphically, some day to day variation in both steroid fractions is seen with all patients, but often these day to day changes are superimposed on longer fluctuations, the rise and fall of which occupy periods from several days to a few weeks. Four lines of enquiry have been followed in an attempt to define the factors influencing adrenocortical function in these patients.

VOL. 5 1960/61

(1) *Relation to the general course of the illness.* Examination of the data graphically does not suggest any general trend in the steroid excretion, which is consistent for the group. Certain patterns do however reflect the course of events in particular cases. For example, steroid excretion in patient No. 3 mirrored the general clinical state throughout an initial period of improvement, a relapse and subsequent recovery. Both fractions were higher during the relapse period of sereral weeks. Similarly, with patient No. 18, in whom anxiety was a marked feature, and who improved rapidly with E.C.T., which was started shortly after admission, the ASFS showed a steady downward trend throughout.

(2) *Relation to E.C.T.* Graphically the data do not demonstrate any consistent change in steroid excretion which could be related to the period of E.C.T. or the period following treatment. The relation of steroid excretion to single shock treatments has therefore been examined as illustrated in Table 3. It is clear that there is no consistent effect which could be attributed to the E.C.T.

TABLE 3—17KS AND ASFS EXCRETION IN RELATION TO E.C.T.
Comparison of E.C.T. days with previous days.
60 treatments on 11 patients.
Changes in excess of 2 mg per 24 hr recorded

17KS			ASFS		
Increase	No change	Decrease	Increase	No change	Decrease
17	31	12	13	34	13

(3) *Relation to mental state and particular clinical events.* In order to examine this relationship the case histories were reviewed to assess exogenous factors which might have played a part in the development or precipitation of the illness. With these facts in mind the medical and nursing notes and the behaviour charts were examined and the times of any disturbing events or changes of mood were noted. Steroid values were examined in relation to these times. Finally, the times of unexplained fluctuations in steroid excretion were examined again in the clinical findings. It is not, of course, to be expected that explanations of all the fluctuations in steroid excretion would be found by this procedure. Such an attempt, if planned, would have involved unnecessary interviews and introspection by the patients, which would have been undesirable. Nevertheless, a sufficient number of correlations (illustrated by Figs. 1–5) were found to suggest two influences. First, that the presence of anxiety or agitation was accompanied by an increase in the corticoid excretion. Second, that clinical events, or preoccupations with a sexual content were associated with increased 17KS excretion. When selected groups of patients in whom such features were marked were compared with others in whom these features were absent or minimal, the findings support these suggestions (Tables 4 and 5).

(4) *The presence of cyclical activity of the adrenal cortex.* Some of the data on adrenocortical activity suggested the possibility of a regular cycle, so that in spite of the variable influences described above, a detailed search for evidence of a cycle was continued. The difficulties involved in handling time series by satisfactory statistical methods, when the series are comparatively short, are considerable, and the majority

of the major fluctuations seen graphically did not appear to follow a regular rhythm. Variograms (JOWETT, 1955) were constructed from the data of one or both steroid fractions on 5 patients. In 4 of these were suggestions of short cycles varying between patients from 5 to 12 days. Artifacts however might result from the fact that occasional weekend values were missing in these series. A fairly long complete series of values from one patient (daily for 72 days) were submitted to a Fourier analysis.

TABLE 4.—17KS EXCRETION IN DEPRESSED PATIENTS PREOCCUPIED WITH SEXUAL PROBLEMS—GROUP A.
Comparison with a selected group free from such problems—Group B.

A Case No.	Age	Normal range for age	Observed range	B Case No.	Age	Normal range for age	Observed range
4	22	7–23	15–35	1	35	7–24	7–20
20	23	7–23	12–27	9	44	6–23	10–18
12	32	8–25	10–22	21	47	5–19	8–14
16	32	8–25	11–20	14	53	4–17	5–13
5	52	4–17	14–32	15	55	4–16	5–9
13	52	4–17	14–27	7	56	3–15	5–14
6	53	4–17	5–22	17	57	3–15	8–14
Wide range with frequent high values				Narrower ranges. All values within normal ranges.			

TABLE 5.—ASFS EXCRETION IN RELATION TO ANXIETY AND AGITATION
Comparison of four depressed patients showing slight or no anxiety nor agitation, with a selected group in which these features were marked.

Marked anxiety		Slight or no anxiety	
No.	Range of ASFS excretion	No.	Range of ASFS excretion
2	2–17	1	6–12 (15)
7	5–18	9	4–11
18	6–25	13	4–8
21	8–20	17	4–9

Normal range for ASFS 3–11 mg per 24 hr.

This suggested a 7-day cycle in the 17KS excretion. In order to inspect the amplitude in absolute values of the possible cycle a Buys Ballot table with seven columns, as suggested by the Fourier spectrograph, was drawn up and the mean values of the resultant peak and trough compared. From this it appeared that the mean daily difference was only just in excess of the 2 mg per 24 hr—a minimal change in terms of the reproducibility of the method when single values are compared. Furthermore, an analysis of variance of the means in the Buys Ballot table showed that the differences were not statistically significant. This does not necessarily negate the suggestion of a

VOL. 5 1960/6

cycle, but emphasises that it would be one of low amplitude. It is possible that cyclical changes of low amplitude, and with a 7-day period, might be artifacts of the weekly routine, and such changes might or might not be present in these patients in situations other than that of a hospital ward.

Regarding the relationship of E.C.T. to adrenocortical activity, it is known that a brief rise of the blood level of 17-hydroxycorticosteroids follows the shock (Bliss *et al.*, 1954). The absence of any increased urinary excretion of glucocorticoids in relation to E.C.T., as reported here, is consistent with this brief rise in the blood level being of little biological significance, and with the view that activation of the adrenal cortex is not part of the therapeutic process initiated by the shock. Indeed, there would seem to be no need for stimulation of the cortex which appears to be responding normally or even to an exaggerated degree to a number of influences which we have attempted to define.

Increased glucocorticoid excretion in relation to anxiety is well recognised. Bliss *et al.* (1956) have drawn attention to the rather modest increases demonstrated in relation to anxiety in the blood levels of 17-hydroxycorticosteroids, which usually remain within normal limits. It may therefore be emphasised that the increases in urinary excretion of ASFS are often considerable giving 24 hr values well beyond the normal range. There is no discrepancy between these findings since these authors studied short-term effects, and high normal blood levels of glucocorticoids, if sustained, may give rise to increased urinary excretion. This does however confirm the view previously expressed that measurement of urinary excretion is the method of choice for assessment of adrenocortical function in serial studies. Little is known, in contrast, of the factors which influence androgen excretion in man. Androgen excretion by the adrenal is usually increased to some extent with the corticoid increase provoked by ACTH, but may also increase independently. The variation which may occur in the testicular component (usually considered to represent approximately 20 per cent of the urinary 17KS) is not known. If the 17KS values are accepted as some indication of androgen activity, then the association demonstrated between sexual preoccupations and increased 17KS excretion appears reasonable on theoretical grounds. It should be noted that in several instances here, increased 17KS excretion was observed independently of any increase in ASFS.

In relation to this group of patients the general point can be made that both glucocorticoid and androgen activity may vary considerably in the course of these illnesses, the variation being related to mood changes and disturbing events or preoccupations. This emphasises the fact that a depressive illness is by no means a negative state from the physiological point of view, nor one in which mood changes do not occur. Previous serial studies of endocrine function in depression have mainly concerned patients with short manic depressive swings (Reiss, 1953; Bryson and Martin, 1954; Rizzo *et al.*, 1954). Glucocorticoid activity has been high in the depressive phase compared with the manic, while the 17KS excretion is described as normal throughout, or increased in the manic phase. These reports have related the steroid values to the predominant mood of these clear cut phases, without particular reference to the variable degree of anxiety in either phase, or the different mental content and preoccupation of the patients. Kraines (1957), however, has stressed the fluctuating course which the descent to and rise from the nadir of a depressive illness follows. He believes that much of the symptomatology at these times is determined by

psychodynamic mechanisms, although the essential depressive features could be attributed to an underlying diencephalic or rhinencephlic dysfunction. It seems likely that the changes in steroid excretion described here reflect this variable course, and are similarly related to changing mental content.

SUMMARY

Serial studies of thyroid and adrenocortical function were made throughout their stay in hospital on a group of male patients suffering from depressive illness.

No specific abnormality or pattern of endocrine activity was found for this group of patients.

Their thyroid function was normal and in most cases stable throughout the course of these illnesses.

Adrenocortical function showed considerable fluctuations indicating that the cortex was reactive in normal or even exaggerated degree.

These fluctuations were not related to the general course of the illness nor to E.C.T. They were related to changes of mood or particular disturbing events. Anxiety and agitation were accompanied by increased corticoid excretion: disturbances with a sexual content were accompanied by increased 17KS excretion.

Suggestions, resulting from variograms and a Fourier analysis, of a regular cycle in the steroid excretion of some patients were not definitely confirmed when the significance of the changes in absolute values was assessed.

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VOL.
5
1960/6

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5
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PSYCHOSOMATIC RESEARCH IN JAPAN*

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THE tendency toward a comprehensive approach to human illness has long existed in Japan under the influence of oriental spiritualism. Not until the end of the Second World War, however, were scientific and experimental methods employed in the study of psychosomatic disorders, chiefly as a result of European and American influences. The psychodynamic approach to neurosis was already well established, and for the purposes of this review it is necessary to consider the activities of the two groups that had made the most significant contributions in this field. The first group, the Freudian analysts, began their work in 1910; the second group followed the ideas of the late Dr. Morita, who developed a unique and indigenous therapy for neurosis about thirty-five years ago.

PSYCHOANALYSIS IN JAPAN

(a) 1910–1929. The psychoanalytic theories of Freud, Jung and Adler were introduced into Japan through various publications.

(b) 1930–1945. Prof. K. Marui and Mr. Y. Yabe introduced psychoanalysis into Japanese Medical Circles after studying in America and England respectively.

(c) In October 1955 the Japanese Psycho-analytical Association was established, and Dr. H. Kozawa was appointed President of the Association. There are now about 300 members; Dr. T. Miura is President. However, Dr. H. Kozawa and Dr. M. Yamamura, both of whom are Freudians, are the only two training analysts in Japan approved by the International Psychoanalytical Association.

MORITA THERAPY

This account is based on Dr. Kondo's paper published in the *American Journal of Psycho-analysis* (68).

According to the Morita school, the anxiety of a neurotic person is caused by his reaction to his unfavorable environment in a specific way. He feels his psychological as well as physiological reactions are special to him and abnormally different from those of others. In contrast, normal people usually show the same or similar reactions but never think or feel that they are of special or abnormal nature. This school enumerates several characteristics of the neurotic personality.

(1) The most outstanding characteristic is hypochondriasis.

(2) Neurotic individuals attempt to make the impossible possible. A neurotic individual, for instance, complains about his difficulty in concentration and asks the doctor to clear out those miscellaneous ideas and images that come in and out of his mind and that prevent him from obtaining a perfect state of concentration. Other neurotics may complain that they cannot attain the absolute or the perfect. It is a matter of simple common sense to understand that this is impossible.

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VOL.
5
1960/6

(3) Neurotic individuals do not want to face anxiety directly. They try to evade, deny, rationalize, or escape from it. It is important to face it, accept it and suffer with it.

(4) Neurotic individuals do not accept facts and learn from them.

(5) Neurotic individuals tend to think of themselves as set apart, and different from others.

(6) Neurotic individuals wish to have happiness without effort.

(7) In contrast to an insistence on absolute perfection, it is a conspicuous fact that every neurotic individual is troubled by a feeling of inferiority or incapacity.

Morita and his followers consider first that learning in and through daily experience is more fundamental and deep than intellectual understanding. Secondly, they prefer a direct approach to the stimulation and development of the constructive force within the patient, rather than the analytic approach to the obstructive, pathological aspects of the patient. The followers of Morita are under the impression that if the constructive force is strengthened and mobilized freely and powerfully, the pathological aspects will fade away.

The following important factors which are utilized for the promotion of the constructive force must also be mentioned. First is the stress on the curative effects of nature; second, emphasis on manual work; and third is the importance of the attitude called "acceptance".

MORITA advises the patient to take reality as it is, accept it and live with it without struggling to evade, escape, or deny it. Acceptance, although it is commonly misunderstood in Western culture which emphasizes activity, is not mere passivity or resignation. It is a realistic attitude consisting of a clear cognizance of the reality of a given situation and the courage to embrace and live with this reality. It is quite a positive attitude and can be called "creative passive-activity". Morita suggests that manual work should be carried out in whatever field the patient feels he likes. At first the patient is always concerned with symptoms, but as he becomes more involved in his work, he seldom pays attention to them, and through this experience in his work he begins to learn how to "accept".

Re-examination of the whole system of Morita therapy in the light of psychoanalysis seems to help this therapy develop more effectively and profoundly.

PSYCHOSOMATIC RESEARCH IN JAPAN 1945-1959

Studies in Experimental Neuroses

Dr. N. YOSHII and his associates induced conditioned fits (audiogenic seizures) in rats, by applying the electrical and audiogenic stimuli simultaneously. They have studied the changes in E.C.G., E.E.G., cerebral and peripheral temperature, and the behaviour pattern of the rats suffering from the experimental neurosis which was induced by repeating the above-mentioned procedure. In addition, the effect of partial decortication and adrenal denervation upon such an experimental neurosis was studied (51, 52, 53, 54, 126, 127, 143, 153, 154, 155).

Dr. K. ASAHINA and his associates induced an experimental neurosis in albino rats by enforced severe exercise (compulsory swimming in a water tank). They found marked histological changes in the brain (particularly in the cerebrum) of those rats suffering from such an experimental neurosis. The changes in the acute stage consist

of swelling of cells followed by atrophic change in the chronic stage. The histological changes in other organs of neurotic rats were similar to those seen in the General Adaptation Syndrome, although they considered that Stress theory alone could not explain such generalized changes (5, 6, 7, 142).

Dr. Y. KOGA and his associates induced emotional stress in rats by means of a special device "Setting a cat on rats" and studied the effect of such emotional stress on the function of the adrenal cortex and the learned behaviour of the animals (43, 65).

The Physiology of Emotions

Dr. T. SAKURAI and his associates found that the intravenous injection of Myanesin (a non narcotic inhibitor of the brain-stem) produced a marked fluctuation in the blood pressure of anxious psychoneurotics, and they considered that the "Myanesin test" could be used as an indication of the progress of neurosis. The changes in blood sugar level and blood water content after the intravenous injection of cariazol (a stimulant to the brain-stem) were also found to be marked in the state of anxiety. As the appearance of such somatic changes precede that of anxiety, they state that "vital" anxiety can be distinguished from the "secondary" anxiety by these methods (32, 76, 109, 112, 122, 124, 152).

Dr. SUWA and his associates have studied the interrelations between variations in the psychic states of patients with neurosis, schizophrenia, manic-depressive psychosis etc. and the changes in various physiological factors, such as the function of the autonomic nervous system, thyroid gland, water-salt-metabolism, biological substances occurring in the urine, eosinophils and abnormal sugar metabolism. The effect of the application of various physical, chemical and emotional stimuli upon the antidiuretic hormone of the posterior pituitary gland was also studied (37, 38, 40, 105, 129, 139, 151).

Other papers on this subject are 16, 44, and 63.

Studies of Bodily Reactions Produced by Experimentally Induced Emotions

I and my associates induced various emotional states by hypnotic suggestions and interview techniques. The effect of emotions induced thus upon the functions of the gastrointestinal system, pituitary adrenocortical axis, autonomic nervous system, cardiovascular system, kidney, antibacterial activity of the blood, blood sugar, urine sugar, acid-base balance, and serum protein fractions have been studied. Among the data obtained by these experiments, we are particularly interested in the remarkable changes in the antibacterial activity of human blood and fractions of serum protein under emotional stress induced by the above-mentioned techniques. Numerous clinical observations on the interrelation between emotions and various neurotic or psychosomatic conditions have also been made by our group (9, 11, 12, 13, 18, 20, 27, 28, 29, 30, 31, 55, 75, 85, 89, 92, 104, 106, 107, 121, 128).

General and Theoretical Remarks on Neurosis and Psychosomatic Disorders

Dr. T. HORIMI and several other workers began to introduce American psychosomatic medicine into Japanese Medical Circles soon after the end of the war. In the meantime, on the basis of the psychosomatic concepts published in *Psychosomatic Medicine* (WEISS and ENGLISH, ALEXANDER), *Emotions and Bodily*

VOL.
5
1960/6

Changes (DUNBAR) and other works, numerous general remarks on these problems have been published. Dr. SCHULTZ's theory concerning neurosis, and his autogenous training was also discussed (23, 35, 46, 49, 50, 74, 94, 98, 100, 117, 125, 138).

Clinical Observations of Neurosis and Psychosomatic Disorders

The abnormality (instability or lowering) of the pituitary-adrenocortical function of psychoneurotics has been pointed out by several research workers and the administration of ACTH, X-ray application to the interbrain or the transplantation of the pituitary gland of a calf have been tried for the treatment of neurotic conditions (3, 108, 116). Dr. K. KUSHIMA and his associates have studied the function of the autonomic nervous system and the psychology of women who complain of angion neurotic or menopausal syndromes and have stressed the psychosomatic aspects of such syndrome. He found a predominantly endocrine cause in most cases, and a psychological cause in others (81, 82, 83). Dr. T. KANEHISA and Dr. S. SUGIMACHI noticed that the lowering of the T complex occasionally seen in the E.K.G. of the patients with cardiac neurosis sometimes disappears after brief psychotherapy (45, 93, 135). Many other clinical and statistical observations on neurotic and psychosomatic conditions are included in the following references (8, 17, 25, 39, 41, 56, 57, 58, 59, 62, 80, 90, 95, 96, 97, 103, 110, 111, 114, 118, 119, 120, 130, 133, 134, 136, 137, 141, 148, 156).

Psychodynamic Study of Neurosis and Psychosomatic Disorders

Dr. KOZAWA and his associates (Dr. K. OKONOGI and other members of the Keio group, Dr. NISHIZONO and others) are faithfully following the lines of orthodox Freudian psycho-analysis. Dr. H. KURAUCHI, Dr. S. MAEDA and others are testing the validity of the psychoanalytical theory of the Freudian school mainly using hypnosis from the standpoint of experimental psychology (77, 78, 79, 86, 113). Dr. M. DOI is making a psychoanalytic study of the cultural characteristics of the Japanese. Dr. OGINO, Dr. DOI and others are beginning the dynamic approach to various psychotic conditions. Many papers on the psychoanalytical study of psychogenic tic, ulcer personality, hypertension, depersonalization, neurosis, bronchial asthma, tuberculosis, attacks of yawning have been published (4, 14, 21, 22, 34, 42, 48, 60, 61, 71, 72, 84, 149, 150).

There is a group of research workers who criticize the theory and method of orthodox Freudianism and are attempting to revise these views. For example Dr. T ABE and others are seeking for a compromise between Morita therapy and psychoanalytic theory (1, 2). Dr. A. KONDO, who studied with Karen Horney, is investigating the interrelation between Neo-Freudian theory and that of Morita Therapy (67). Dr. T. KORA, Dr. K. IKEDA and others are studying the clinical application of Morita therapy to many cases of so called Morita nervousness (26, 73). Dr. K. KAKETA suggests that psychotherapy in Japan will go in the direction of the integration of psycho-analysis and Morita Therapy.

Studies of Clinical Psychology

The Rorschach test, the Thematic Apperception test, Cornell Medical Index, Minnesota Multiphasic Personality Inventory etc. are being used clinically and for the purpose of psychosomatic research (10, 15, 24, 115, 140). The socio-psychological

approach to neurotic and psychosomatic conditions has recently been initiated by Dr. T. KANEHISA and others (47).

Studies of the Constitutional Factors in Neurotic and Psychosomatic Syndromes

The abnormality in the function of the autonomic nervous system has been noticed in problem children and juvenile delinquents by a few research workers (36, 91). Dr. Y. KOGA states that patients with early pulmonary tuberculosis sometimes complain of neurotic symptoms such as lassitude, asthenia, loss of weight, and points out that these symptoms can be cured only by antituberculosis drugs. He named such a condition "Camouflaged tuberculosis with neurotic syndrome" (64, 66).

Dr. M. MAEKAWA and his associates noticed the existence of subclinical arachinoiditis in cases with neurotic syndromes (particularly, cardiac neurosis and anxiety neurosis) and found that symptoms vary according to the degree of such a pathological change in the spinal cord. Such a relationship has been found in some cases of psychosomatic disorders such as bronchial asthma and peptic ulcer. He suggests that the problem of "organ choice" in psychosomatic conditions can be partially solved from such a viewpoint (19, 69, 70, 87, 88, 146, 147).

Studies of Conditioned-Reflexes in Connection with Psychosomatic Medicine

The relationship between conditioned behaviour in albino rats, the E.E.G. and the conditioned-reflex of intestinal absorption in rats etc. has been studied (144, 145). The studies on the psychophysiological mechanism of neurotic conditions through the conditioning by GSR and the occurrence of hypoglycemia by the conditioned-reflex in psychotic patients have been published (33, 132).

The Biochemical Approach to Neurosis and Psychosomatic Disorders

Studies on pharmacotherapy for neurosis and psychosomatic disorders are numerous. Dr. S. NAKA and others attach importance to neuro-biochemical mechanisms (101, 102, 123, 131).

Finally, the Japanese Psychosomatic Society has recently been formed. Its members are physicians of various clinical departments, research workers in the basic medical sciences, psychiatrists, psycho-analysts and psychologists. The first annual meeting of this society is to be held in Tokyo in May 1960.

(Almost all the papers mentioned above are written in Japanese. Anyone wishing to know more about any of these works, should communicate with us, and we shall be happy to ask the author to provide an English translation of his work.)

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VOL.
5
1960/6

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VOL.
5
1960/6

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VOL.
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1960/6

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THE INFLUENCE OF SODIUM AMYTAL ON THE RESPIRATORY ABNORMALITIES OF ANXIOUS PSYCHIATRIC PATIENTS*

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WE HAVE previously described the abnormalities shown by anxious psychiatric patients when their respiratory activity is measured successively lying down, standing, performing a standard step exercise and then immediately after exercise in the lying position. Anxious patients expend more energy during and immediately after exercise than do normal subjects. Again, the respiratory efficiency (as defined below) of the patients is impaired in all positions except during and immediately after exercise. These abnormalities disappear or diminish with clinical improvement (MEZEY and COPPEN, 1961).

The following investigation was undertaken to test the hypothesis that these respiratory abnormalities were related to the anxiety shown by the patients and not to other features of the mental illness. It was proposed therefore to reduce the level of anxiety present in these patients by administering sodium amytal (amylobarbitone sodium) and to compare the patient's performance before and after receiving the drug. Sodium amytal is widely used in clinical practice to reduce anxiety and its action is prompt and with no undesirable side effects.

VOL.
5
1960/6

MATERIAL AND METHODS

Eighteen physically healthy patients, 10 men and 8 women, were tested. They were all suffering from affective disorders in which anxiety was a prominent symptom. The length of illness prior to testing was in every case less than 3 months. The patients were tested within a week of their admission to hospital before treatment was started. Nineteen healthy control subjects, 11 women and 8 men, were tested concurrently with these patients. They were paid volunteers, for the most part sedentary office workers, whose age and weight were comparable to that of the patients.

The test was performed in the morning with the patient in a basal state. After half-an-hour at rest on a couch the metabolic rate was measured in the following positions:—(1) in the lying position for 10 min, (2) in the standing position for 5 min, (3) during exercise for 5 min; (4) and (5) were two 5-min measurements made sucessively on lying down immediately after the exercise period. The measurement in the standing position was taken after the subject had spent an initial 5 min in this position in order to reach a steady state after getting up. The standard exercise used was a modification of the Harvard step test in which the subject was asked to step on or off a 22 cm high platform every 3 sec.

Immediately at the end of the test the subjects were given 0·2 g sodium amytal by mouth and they returned to rest on the couch. The test procedure described above was then repeated 45 min after taking the drug. At this stage most subjects described themselves as pleasantly relaxed and some felt drowsy, but they were kept awake by casual conversation.

Respiratory volumes were measured and samples of expired air were collected by means of a close fitting face mask connected to the Integrating Motor Pneumotachograph (WOLFF, 1958). Gas analyses of the samples were made by the SCHOLANDER (1947) method.

* This investigation was carried out with the aid of a grant from The Ford Foundation.

† From the Institute of Psychiatry, The University of London, The Bethlem Royal and Maudsley Hospitals, London S.E.5.

The measure of respiratory efficiency was the ventilatory equivalent (V.E.). The V.E. is obtained from the following ratio:-

$$\frac{\text{total ventilation (l. per min)}}{\text{total oxygen extracted (100 ml per min)}}$$

This index is a measure of the respiratory effort required by the subject to extract 100 ml of oxygen from the respired air and it is generally regarded as a good measure of respiratory efficiency (GRODINS, 1950). Metabolic rates were calculated with WEIR's (1949) technique and expressed as Calories per square metre body surface/min (Cal/m²/min).

The subjects and methods are described in greater detail elsewhere (MEZEY and COPPEN, 1961).

TABLE 1.—VENTILATORY EQUIVALENTS OF CONTROLS AND PATIENTS BEFORE AND AFTER THE ADMINISTRATION OF SODIUM AMYTAL.

Group	*N*	Ventilatory equivalent Ventilation (l.) to extract 100 ml of O_2 from respired air									
		Resting		Standing		Exercise		Recovery (A)		Recovery (B)	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Controls before amytal	19	2·43	0·25	2·77	0·55	2·25	0·31	2·19	0·29	2·73	0·36
Controls after amytal	19	2·53	0·26	2·86	0·42	2·25	0·38	2·12	0·33	2·81	0·43
Patients before amytal†	18	3·27*	1·29	3·46*	0·91	2·62	1·11	2·64	0·88	3·40*	1·30
Patients after amytal	18	2·91	0·31	3·29	0·45	2·75	0·69	2·39	0·28	3·09	0·46

* Differs significantly ($P < 0·05$) from the control patients in the corresponding position, before the administration of sodium amytal.

† Patients have a significantly higher ($P < 0·05$) ventilatory equivalent before than after the administration of sodium amytal.

TABLE 2.—METABOLIC RATES OF CONTROLS AND PATIENTS BEFORE AND AFTER THE ADMINISTRATION OF SODIUM AMYTAL.

Group	*N*	Metabolic rate (Cal/m²/min)									
		Resting		Standing		Exercise		Recovery (A)		Recovery (B)	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Controls before amytal	19	0·680	0·108	0·773	0·122	1·611	0·284	1·204	0·228	0·750	0·130
Controls after amytal	19	0·653	0·130	0·795	0·151	1·516	0·267	1·271	0·181	0·688	0·153
Patients before amytal	18	0·733	0·110	0·839	0·181	1·875*	0·349	1·356*	0·253	0·789	0·168
Patients after amytal	18	0·665	0·115	0·805	0·135	1·617†	0·284	1·256	0·225	0·710	0·131

* Differ significantly ($P < 0·05$) from the control patients, in the corresponding position, before the administration of sodium amytal.

† Patients had a significantly ($P < 0·05$) lower metabolic rate during exercise following the administration of sodium amytal compared to their performance without the drug.

RESULTS

These are shown in Tables 1 and 2.

Before taking sodium amytal the V.E. of anxious patients was found to be significantly higher than that of the control subjects lying down, standing and during the second 5-min period following exercise (B). This implies that the patients had an impaired respiratory efficiency in these positions. The mean metabolic rate of the

patients was significantly higher than that of the controls during exercise and in the first 5 min following exercise (A). This is most marked during exercise when the patients expended some 16 per cent more energy in performing the standard exercise than did the controls.

When tested after taking sodium amytal the anxious patients showed a significant shift in their V.E. (taking all test stages together) towards the control values. The control subjects failed to show any significant change in V.E. after sodium amytal.

After taking the drug the excessive energy expenditure of anxious patients during the exercise period is significantly reduced towards the level of the control subjects before taking sodium amytal. The energy expenditure of the patients is reduced in all other positions, although not to a statistically significant extent. The control subjects show little change in metabolic rate after taking sodium amytal.

DISCUSSION

The results indicate that sodium amytal in non-hypnotic doses causes a temporary reversal of the respiratory abnormalities observed in anxious mental patients. Their respiratory adaptation, under the conditions of the experiment, becomes similar to that found in normal subjects, or indeed in these patients themselves after clinical recovery (MEZEY and COPPEN, 1961). It is known that sodium amytal is a very effective drug for reducing anxiety (SARGANT and SLATER, 1954) and this was confirmed by the patients in the present investigation. It seems reasonable to suppose therefore that the respiratory abnormalities in these patients is dependent on their anxiety and that the improvement in respiratory adaptation is a result of pharmacologically relieving their anxiety.

The physiological basis of the respiratory abnormalities observed in these patients is unknown and thus the mechanism of the improvement effected by sodium amytal must remain speculative. It has been shown that anxious mental patients have excessive neuromuscular activity (SAINSBURY and GIBSON, 1954). It is possible therefore that sodium amytal lowers the neuromuscular activity in these patients towards normal levels and that in consequence the energy expenditure in response to exercise becomes more economic. However it may be that anxiety exerts its effect on respiration centrally and that the temporary improvement brought about by sodium amytal is due to its action on the central rather than the peripheral nervous system.

SUMMARY

The respiratory efficiency and energy expenditure of 18 anxious mental patients and 19 healthy subjects was measured successively when lying, standing, during and immediately after exercise. The anxious patients had a lower respiratory efficiency than the normals in all but the exercise and early recovery period when their energy expenditure was significantly higher than in the normal subjects. The subjects in both groups were immediately given 0·2 g sodium amytal and the test repeated. The control group's performance in the test was little changed but the anxious patients' respiratory efficiency showed a significant shift towards normal and their energy expenditure was reduced, coming very close to the values obtained for the control group.

It was concluded that the anxiety present in these patients was responsible for their respiratory abnormalities.

VOL.
5
1960/6

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METABOLIC EFFECT OF VENEPUNCTURE IN MAN*

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WE HAVE recently reported the presence of respiratory abnormalities in psychiatric patients with marked anxiety symptoms (MEZEY and COPPEN, 1961). When compared with normal subjects, and with themselves when clinically improved, anxious patients have higher metabolic rates, both at rest and, more markedly, during exercise. These patients also have impaired respiratory efficiency, the extraction of oxygen from respired air being significantly less than in normal subjects.

Since it is not known whether these respiratory anomalies are a normal accompaniment of fear and pain, or specific to morbid anxiety states, the present investigation was undertaken to examine the respiratory effects of an unpleasant and slightly painful stimulus in healthy, mentally normal subjects. The stimulus chosen was a venepuncture and the injection of 5 ml of normal saline. This procedure was regarded by the subjects, all medical practitioners, as a mildly disquieting experience.

As the initial part of the experiment showed that the venepuncture resulted in a rise in metabolic rate, two further tests were carried out to elucidate the mechanism of this increase. It was hypothesised that the venepuncture stimulated the release of adrenaline and that it was the calorigenic effect of this hormone (ELLIS, 1956) that was responsible for the rise in metabolic rate. As dihydroergotamine inhibits this action of adrenaline (GRIFFITHS, 1951; ROTHLIN and CERLETTI, 1952) a series of tests was performed after the subjects had received this drug. It was further hypothesised that, if the emotional reaction of normal subjects to venepuncture is physiologically identical to morbid anxiety, the rise in metabolic rate should be prevented or attenuated by amylobarbitone sodium (COPPEN and MEZEY, 1960); in another series of tests a group of subjects was therefore sedated with this drug before the venepuncture took place.

METHODS

Twelve physically healthy volunteers were tested. The test was performed in the morning after the patient had fasted overnight and had rested in a lying position for 30 min on a bed. The metabolic rate was then estimated for 10 min to obtain a basal reading. The subject was then given an intravenous injection of 5 ml of normal saline and further estimations of metabolic rate were then taken at the following times after venepuncture: (a) 0–5; (b) 6–10; (c) 11–15; (d) 16–20; and (e) 21–25 min. The test was repeated on two groups of 6 subjects each; the first group took 2 mg dihydroergotamine methanesulphonate orally, and the second 0·2 g amylobarbitone sodium orally, 45 min before the venepuncture.

Respiratory volumes were measured and samples of expired air were collected by means of a close fitting face mask connected to the Integrating Motor Pneumotachograph (WOLFF, 1958). Gas analyses of the samples were made by the Scholander method (SCHOLANDER, 1947). Metabolic rates were calculated with WEIR's (1949) technique and expressed as Calories per square metre of body surface per min (Cal/m²/min). The ventilatory equivalent was also estimated for each period. This index is a measure of respiratory efficiency and represents pulmonary ventilation (in litres) required for the subject to extract 100 ml oxygen from the respired air. The method is described in greater detail elsewhere (MEZEY and COPPEN, 1961).

* This investigation was carried out with the aid of a grant from The Ford Foundation.

† From the Institute of Psychiatry, The University of London, The Bethlem Royal and Maudsley Hospitals, London S.E.5.

VOL.
5
1960/6

RESULTS

These are shown in Tables 1, 2 and 3.

There is a significant increase in metabolic rate in the 5 min following the venepuncture, the change from the mean basal level being 11·4 per cent. The mean metabolic rate in the subsequent estimation then drops but does not quite return to the basal level.

TABLE 1.—EFFECT OF VENEPUNCTURE ON METABOLIC RATE AND VENTILATORY EQUIVALENT

Subject	Metabolic rate (Cal per m²/min) min after venepuncture					Ventilatory equivalent (Ventilation (l.) to extract 100 ml of O_2 from respired air) min after venepuncture				
	Basal Level	0–5	6–10	11–15	21–25	Basal Level	0–5	6–10	11–15	21–25
1	0·827	0·841	—	0·778	0·784	2·01	2·26	—	2·30	2·00
2	0·646	0·768	—	0·628	0·660	2·87	2·13	—	2·56	2·42
3	0·638	0·692	—	0·531	0·586	2·05	2·16	—	2·40	2·17
4	0·613	0·659	0·594	0·616	0·591	2·56	2·63	2·76	2·53	2·41
5	0·651	0·770	0·803	—	0·824	1·95	2·24	1·81	—	1·81
6	0·681	0·710	0·692	—	0·672	1·87	2·03	2·03	—	1·78
7	0·739	0·792	0·620	—	0·692	2·37	2·50	2·62	—	2·46
8	0·592	0·804	0·745	0·795	0·669	2·64	2·45	2·42	2·26	2·41
9	0·685	0·828	—	0·644	—	2·17	1·97	—	2·42	—
10	0·482	0·555	0·575	0·573	—	2·24	3·01	2·58	2·67	—
11	0·772	0·760	0·804	0·793	0·823	2·29	2·29	2·17	2·23	2·22
12	0·596	0·638	0·682	0·643	0·584	2·54	2·11	2·26	2·42	3·07
Mean	0·660	0·735*	0·689	0·667	0·689	2·30	2·32	2·33	2·43	2·28
Change from mean basal level in per cent		+11·4	+4·4	+1·1	+4·4					

* Mean value of metabolic rate 0–5 min after venepuncture differs significantly from the basal mean values ($t = 4{\cdot}43$, $P < 0{\cdot}01$).

Dihydroergotamine modified the effect of venepuncture and during the following 5 min there was a slight decrease in the mean metabolic rate which remained substantially unchanged throughout the subsequent estimations. The administration of amylobarbitone sodium does not affect the metabolic response to venepuncture; the subjects showed a mean increase of 9·4 per cent over the basal level during the 5 min following the venepuncture.

Throughout the three sets of experiments the ventilatory equivalent showed little change.

DISCUSSION

A venepuncture and the injection of a small amount of saline caused an immediate rise in the metabolic rate of normal subjects. This effect is similar to that found by LUNDHOLM (1949) in animals after infusions of adrenaline in moderate doses and attributed by him to emptying of the blood depots and oxygenation of their venous

TABLE 2.—EFFECT OF VENEPUNCTURE ON METABOLIC RATE AND VENTILATORY EQUIVALENT, AFTER THE ADMINISTRATION OF DIHYDROERGOTAMINE, 2 MG

Subject	Metabolic rate (Cal per m²/min) min after venepuncture					Ventilatory equivalent (Ventilation (l.) to extract 100 ml of O_2 from respired air) min after venepuncture				
	Basal level	0–5	6–10	11–15	21–25	Basal level	0–5	6–10	11–15	21–25
1	0·764	0·655	0·936	0·717	0·848	1·89	1·89	2·07	1·84	1·82
2	0·786	0·817	0·697	0·768	0·696	2·81	2·41	2·75	3·06	2·87
3	0·772	0·753	0·796	0·750	0·757	2·50	2·57	2·58	2·38	2·34
4	0·647	0·586	0·603	0·608	0·619	2·51	2·36	1·94	2·58	2·22
5	0·726	0·813	0·665	0·720	0·709	2·38	2·16	2·37	2·20	2·36
6	0·718	0·694	0·755	0·755	0·730	1·84	1·88	1·77	2·00	1·67
Mean	0·735	0·720	0·742	0·703	0·727	2·32	2·21	2·25	2·34	2·21
Change from mean basal level in per cent		−2·04	+0·95	−4·4	−1·10					

TABLE 3.—EFFECT OF VENEPUNCTURE ON METABOLIC RATE AND VENTILATORY EQUIVALENT, AFTER THE ADMINISTRATION OF AMYLOBARBITONE SODIUM 0·2 g.

Subject	Metabolic rate (Cal per m²/min) min after venepuncture					Ventilatory Equivalent (Ventilation (l.) to extract 100 ml of O_2 from respired air) min after venepuncture				
	Basal level	0–5	6–10	11–15	21–25	Basal level	0–5	6–10	11–15	21–25
1	0·529	0·648	0·718	0·661	0·565	2·58	2·63	2·18	2·38	2·38
2	0·634	0·672	0·552	0·685	0·623	2·39	2·39	2·49	2·39	2·32
3	0·757	0·714	0·735	0·703	0·669	2·79	2·87	2·68	2·87	2·87
4	0·701	0·792	0·691	0·614	0·662	2·22	1·90	2·30	2·31	1·97
5	0·623	0·716	0·614	0·631	0·591	2·07	2·37	2·58	2·57	2·31
6	0·559	0·631	0·629	0·668	0·694	2·27	2·49	2·38	2·62	2·57
Mean	0·634	0·696	0·657	0·660	0·634	2·39	2·44	2·44	2·52	2·40
Change from mean basal level in per cent		+9·8	+3·6	+4·1	0					

blood. The abolition of this response by dihydroergotamine, which inhibits the calorigenic action of adrenaline, supports the view that it is due to adrenergic substances.

The rise in metabolic rate is not accompanied by any impairment of the ventilatory efficiency which remains unchanged throughout the experiment. The mechanism of the increased energy expenditure in healthy subjects after the mild discomfort of a

VOL. 5 1960/6

venepuncture differs therefore from that observed in patients with morbid anxiety. Another difference between the two groups lies in their response to amylobarbitone sodium which improved the respiratory performance of the anxious patients but did not affect the response of normal subjects to venepuncture.

SUMMARY

The metabolic effect of a venepuncture and injection of normal saline was measured in 12 normal subjects. In the 5 min following the venepuncture there was a 11·4 per cent rise in the metabolic rate above the basal level. This response was inhibited by dihydroergotamine, but not by amylobarbitone sodium. It was concluded that the rise was due to the calorigenic effect of adrenaline released as a result of the painful stimulus of the venepuncture.

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THE INFLUENCE OF ISOPRENALINE AND PREDNISONE ON THE RESPIRATORY ADAPTATION OF NORMAL SUBJECTS*

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ABNORMALITIES of the respiratory adaptation of anxious psychiatric patients and the respiratory effects of a painful stimulus on healthy normal subjects have been described in previous papers (MEZEY and MELVILLE, 1960; MEZEY and COPPEN, 1961; COPPEN and MEZEY, 1960a). The respiratory changes in the two groups differed and those observed in the anxious psychiatric patients were inhibited by amylobarbitone sodium which did not effect the response of the normal subjects. The reaction of the painful stimulus was however inhibited by dihydroergotamine (COPPEN and MEZEY, 1960b).

It has been frequently reported that increased adrenergic (ELMADJIAN, 1959) and adrenocortical activity (PERSKY *et al.*, 1959) accompany emotional states characterised by anticipation and mental tension, and we postulated that the respiratory abnormalities observed in pathological anxiety are secondary to the high level of these hormones in circulation. We proposed therefore to investigate the respiratory effects of isoprenaline, a synthetic adrenergic agent of prompt action (LANDS *et al.*, 1947), and of prednisone, a synthetic substance with cortisone-like properties (BOLAND, 1955).

MATERIAL AND METHODS

As a detailed description of the experimental procedure and methods will be found elsewhere (MEZEY and COPPEN, 1961), these are only outlined here.

Eleven healthy normal subjects were tested in the basal state and after an initial rest of 30 min on a couch. The test consisted of five stages, with the subject (1) lying down; (2) standing at ease; (3) performing a step test; (4) and (5) lying down. The Integrating Motor Pneumotachograph (WOLFF, 1958) was used for the measurement of respiratory volumes and collection of air samples which were analysed by the SCHOLANDER (1947) technique. Metabolic rates were expressed as Calories per square metre of body surface/min (Cal per m^2/min) and the ventilatory equivalent (V.E.) was taken as a measure of the respiratory efficiency.

The effect of isoprenaline was tested in six experiments in the following way: after resting for 60 min at the end of the first test, the subject took 10–20 mg isoprenaline sublingually and 2 min later the test was repeated.

Six other subjects repeated the test a few days later, after the administration of prednisone. Three took 10 mg prednisone orally the night before, and the same dose again in the morning, 60 min before the start of the test; the other 3 took 5 mg prednisone daily for 4 days, the last dose being taken the morning on which the test took place.

RESULTS

These are shown in Tables 1–4.

After isoprenaline the energy expenditure showed a general and highly significant increase, with a rise of over 32 per cent in metabolic rate during stepping. The

* This investigation was carried out with the aid of a grant from The Ford Foundation.

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VOL. 5 1960/6

TABLE 1.—EFFECT OF ISOPRENALINE ON METABOLIC RATE
(Cal per m²/min)

		Control					Isoprenaline				
		Position					Position				
Iso-prenaline (mg)	Subjects	1	2	3	4	5	1	2	3	4	5
10	A	0·578	0·669	1·290	1·010	0·772	0·695	1·006	1·714	1·245	0·713
20	A	0·578	0·669	1·290	1·010	0·772	0·873	1·017	2·150	1·152	0·739
20	B	0·707	0·584	1·757	—	0·591	0·837	0·901	2·420	1·253	0·867
20	C	0·864	0·712	1·527	1·224	0·609	0·651	0·958	1·680	1·166	—
10	D	0·572	0·761	1·715	1·102	0·728	0·707	0·885	2·027	1·253	0·828
20	E	0·840	1·100	1·573	0·763	0·780	0·755	0·856	2·106	1·219	0·677
	Mean	0·660	0·749	1·525	1·022	0·709	0·753	0·937	2·016	1·215	0·765
	Percentage change in mean after isoprenaline						+14·1	+25·1	+32·2	+18·9	+7·9

Comparing all positions before and after isoprenaline, $t = 4{\cdot}48$, $P < 0{\cdot}001$.

TABLE 2.—EFFECT OF ISOPRENALINE ON THE V.E.
(ventilation (l) to extract 100 ml of O_2 from respired air)

		Control					Isoprenaline				
		Position					Position				
Iso-prenaline (mg)	Subjects	1	2	3	4	5	1	2	3	4	5
10	A	2·11	3·02	2·52	2·13	2·17	2·31	2·20	2·53	1·74	2·45
20	A	2·11	3·02	2·52	2·13	2·17	2·73	2·50	2·37	1·95	2·29
20	B	2·48	3·00	2·03	—	3·25	2·99	3·02	2·07	2·80	3·12
20	C	2·26	2·34	1·69	1·85	2·67	2·89	2·08	2·00	2·31	—
10	D	2·34	2·94	2·81	1·71	2·24	2·74	2·80	2·40	2·25	2·80
20	E	2·00	2·31	2·29	3·07	2·48	2·45	3·11	2·59	3·15	2·24
	Mean	2·22	2·77	2·31	2·18	2·50	2·69	2·62	2·33	2·37	2·58
	Percentage change in mean after isoprenaline						+21·2	−5·4	+0·9	+8·7	+3·2

Comparing all positions before and after isoprenaline, $t = 2{\cdot}05$, $P < 0{\cdot}05$.

Table 3.—Effect of prednisone on metabolic rate
(Cal per m²/min)

		Control					Prednisone				
		Position					Position				
	Subjects	1	2	3	4	5	1	2	3	4	5
Prednisone 20 mg in 12 hr	F	0·572	0·761	1·715	1·102	0·728	0·573	0·647	1·442	1·100	0·665
	G	0·603	0·627	1·704	1·244	0·682	0·624	0·615	1·526	1·104	0·691
	H	0·684	0·712	1·527	1·224	0·609	0·686	0·746	1·521	1·167	0·598
	Mean	0·619	0·700	1·649	1·190	0·673	0·627	0·667	1·476	1·123	0·651
	Percentage change in mean after prednisone						+1·2	−4·8	−9·3	−5·7	+3·8
Prednisone 20 mg in 4 days	I	0·578	0·669	1·290	1·010	0·772	0·785	1·008	1·789	1·704	0·894
	J	0·840	1·100	1·573	0·763	0·780	0·777	0·671	1·940	1·342	0·713
	K	0·863	0·860	1·460	1·242	0·789	0·642	0·626	2·222	1·100	0·739
	Mean	0·760	0·876	1·441	1·002	0·780	0·734	0·768	1·983	1·382	0·782
	Percentage change in mean after prednisone						−3·5	−12·3	+37·6	+37·5	−0·3

Table 4.—Effect of prednisone on the V.E.
(ventilation (l.) to extract 100 ml of O_2 from respired air)

		Control					Prednisone				
		Position					Position				
	Subjects	1	2	3	4	5	1	2	3	4	5
Prednisone 20 mg in 12 hr	F	2·37	2·63	1·85	2·25	2·29	2·40	2·70	1·99	2·09	2·31
	G	2·55	2·85	1·87	2·26	2·57	2·51	2·71	2·08	2·13	2·25
	H	2·26	2·34	1·69	1·85	2·67	2·43	3·72	1·70	2·01	2·76
	Mean	2·39	2·60	1·80	2·12	2·51	2·45	3·04	1·92	2·07	2·45
	Percentage change in mean after prednisone						+2·5	+16·9	+6·6	−2·4	−2·4
Prednisone 20 mg in 4 days	I	2·11	3·02	2·52	2·13	2·17	2·89	2·63	2·56	1·54	2·60
	J	2·00	2·31	2·29	3·07	2·48	2·15	3·12	2·17	2·00	2·45
	K	2·36	2·76	2·37	2·34	3·01	2·60	3·28	1·93	2·54	2·49
	Mean	2·15	2·70	2·39	2·52	2·55	2·54	3·01	2·22	2·02	2·52
	Percentage change in mean after prednisone						+18·1	+12·7	−6·4	−19·9	−1·2

VOL.
5
1960/6

changes in ventilatory equivalent were less marked or constant, the increase just reaching significance level for the whole test.

The three subjects who took prednisone only during the 12 hr immediately preceding the test showed little alteration in metabolic rate; the ventilatory equivalent showed a marked rise in the standing position, but not for the other stages of the test. The other 3 subjects who took the drug for over 4 days showed considerable changes in their metabolic rate, which became lowered in standing, while it rose during and immediately following exercise by about a third over the control figures; the ventilatory equivalent of these subjects increased at rest, whether lying or standing.

DISCUSSION

The changes in respiratory adaptation following isoprenaline do not closely resemble the abnormalities we have previously reported in anxious psychiatric patients. The overall increase in energy expenditure, accompanied by an inconsistent and only moderate impairment of respiratory efficiency, are similar to the effects of venepuncture in healthy normal subjects (COPPEN and MEZEY, 1960b) and confirm indirectly that the latter were caused by liberation of adrenergic substances.

The short-term administration of prednisone had no definite effect on respiratory adaptation, with the possible exception of the impaired respiratory efficiency during standing. Following the more prolonged use of the drug, there was an increase in energy expenditure during exercise and the first five minutes of the recovery period, with an impaired ventilatory efficiency when lying and standing up. These findings are strikingly similar to those found in pathological anxiety and suggest that in the latter the respiratory changes were secondary to sustained adrenocortical hyperactivity.

Confirmation of our findings on a larger experimental population and the investigation of the effects of simultaneous administration of adrenergic substances and adrenocortical hormones might shed further light on the pathological physiology of morbid anxiety.

SUMMARY

The effects of isoprenaline and prednisone on the respiratory adaptation to exercise of 11 healthy normal subjects have been investigated.

Isoprenaline causes a general increase of energy expenditure. Prolonged administration of prednisone is followed by a marked rise of energy expenditure during and immediately following exercise, with an impaired respiratory efficiency at rest, whether lying or standing. These effects of prednisone closely resemble the respiratory abnormalities of anxious psychiatric patients.

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VOL.
5
1960/6

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BOOK REVIEWS

Schizophrenia. A Review of the Syndrome. Edited by LEOPOLD BELLAK. Logos Press, New York, 1958. 1010 pp., $14.75.

IN 1948, in his book 'Dementia Praecox,' Dr. BELLAK was able, single handed, to review the literature on schizophrenia published between 1936 and 1946. Now, ten years later, he has had to acknowledge that the task has got beyond the scope of one man. With a team of 21 collaborators he has produced a magnificent compendium of the literature (there are over 4,000 references). Every aspect of the syndrome is adequately considered, and the different contributions are remarkably free from bias. A good index is essential for what is, in effect, a reference book, and it does not disappoint. This is an invaluable book for any psychiatrist, and Dr. BELLAK has carried out his monumental task in a truly admirable manner. The price is not excessive.

DENIS LEIGH

Instinctive behaviour: The development of a modern concept. Translated and edited by H. CLAIRE SCHILLER. Methuen, 1957. 328 pp., 45s.

DECIDING the relevance to psychosomatic research of the results of studies using infra-human animals is complicated by the existence of two alternative disciplines which claim to have something to offer in this direction, and which have different techniques, theories and even objects of study. They are comparative psychology and comparative ethology. This book represents the point of view of the latter, while your reviewer's affiliations have been with the former. The two disciplines are well contrasted by TINBERGEN in his foreword, in which he struggles to be impartial in distinguishing between them. Comparative psychologists have tended to be American, to have written in English, and to have studied problems relating to learning, and to have done so especially in mammals, using in preference to all other species, the rat. Comparative ethologists, on the other hand, who are zoologists, have tended to be European, to have written in German and to have studied problems relating to innate behaviour in a wide range of fish, insects and especially birds.

The virtue of this book is that it presents for the first time in English a collection of some of the more important papers in the history of the development of the theoretical constructs used by the ethologists. It is thus likely to be of use in furthering understanding of these constructs and aiding that integration of the two disciplines which each claims to desire. The papers translated range from VON UEXKÜLL's 1934 'Stroll through the worlds of animals and men', with its clever, if sometimes fanciful, evocation of the perceptual world of animals and insects, to LORENZ's hard-headed 1952 review of the past twelve years' developments in comparative ethology. In this paper LORENZ is justly proud of the achievements of the ethological approach, but almost wistfully notes the increasing complexity of the theoretical ideas then developing in comparative ethology. This process has subsequently been carried further, and has reached a point where critics have come to question the usefulness of some of them, for example the innate releasing mechanism or IRM, so hedged about with limitations have they become. But in this book no such doubts appear, for the papers intervening between the first and the last—papers by LORENZ himself, by TINBERGEN, KUENEN and SCHILLER—date principally from the 1930's and display the freshness and enthusiasm of the new approach to the study of instinctive behaviour. Most of the studies reported are on birds; it is perhaps characteristic of comparative ethology that the one paper on mammals (on chimpanzees, by SCHILLER) is the least convincing. The papers yield some of the earliest examples of that ingenuity of experimentation, especially in the field, for which the ethologists have come to be noted, together with some examples of that lack of rigour in reporting and interpreting their results which has laid them open to censure,

though, happily, less frequently in the more recent past. Here we can see the beginnings and the early development of the concepts of the innate releasing mechanism, of vacuum activities—the discharge of the mechanism in the absence of the appropriate stimulation or releaser—and of taxes or orienting mechanisms.

Perusal of a book of this kind prompts the question: to what extent are these concepts helpful in comprehending the problems raised by psychosomatic disorder? It seems axiomatic that the greater dependence of human activity on learned as opposed to innate responses must lessen their usefulness and correspondingly increase that of concepts derived from the study of learning. The existence of a well-developed theory of learning and some recent successes in applying it therapeutically to some limited psychosomatic symptoms may reinforce this view. This is not to say that genetically determined mechanisms of the sort that LORENZ and the other contributors to this book have studied in lower animals do not exist in man; they almost certainly do, and many human individual differences probably owe much to genetic determinants. It is rather to say that such determinants are more likely to control predisposition rather than expression. The expression itself is partly overlaid with, and its precise mode so largely determined by, learned responses that it is on them that our endeavours at present seem best concentrated.

P. L. BROADHURST

H. J. EYSENCK: **The Manual of the Maudsley Personality Inventory.** University of London Press, London, 1959, 2/6d.

THIS 48-item questionnaire was designed to measure neuroticism (or emotional instability) and extraversion-introversion.

The Inventory has been given to normal subjects, Hysterics, Dysthymics, Psychopaths (in Hospital), Prisoners and Psychosomatic cases.

Split half and re-test reliabilities appear to average just above 0·8 for both scales.

The standardization data call for some comment. Neurotics were diagnosed by experienced psychiatrists, or else had their case-papers carefully scrutinized by three experienced clinical psychologists, who arrived at a unanimous diagnosis independently. In his reply (*J. abnorm. soc. Psychol.* 1958, **57**, 2) to the paper by SIGAL, STARR and FRANKS (*ibid*) EYSENCK rather deplores the latter method. It is unfortunate that their somewhat conflicting results were not available for the Manual, since the claim that 'successive samples from different hospitals showed great stability in means and variances' might have required some modification.

EYSENCK believes that the results obtained on the M.P.I. 'in a sense . . . serve as validation of the scales'. This, unfortunately, can only be in an illogical sense. It is not possible to validate the theory and the inventory at the same time. It would be palpably absurd to claim—and certainly JUNG did not—that Hysteria and Extraversion are one and the same thing. What JUNG said, in effect, was most neurotic extraverts have the characteristics of Hysteria; most neurotic introverts have the characteristics of Dysthymia. A demonstration of differences between Hysteria and Dysthymia does not necessarily tell us anything at all about extraversion : introversion. The differences in the particular instance may be due to quite other characteristics. The M.P.I. has, of course, considerable face-validity for at least some aspects, particularly social, of that elusive concept extraversion. It is doubtful whether reliance on 'construct validity' is of any value when there is a large logical hole in the nomological network.

In respect of the extraversion : introversion continuum, the position of the recidivist prisoners and the psycho-somatic cases is close to the hysterics, a finding which to EYSENCK is not unexpected. The reviewer would have expected recidivist prisoners to be closer to hospital psychopaths than to hysterics. With regard to the psycho-somatic group, at least one large sub-group consists of people whose intense affective disturbance has resulted in physiological changes such as are rare in hysteria. If STANLEY COBB's two broad categories are correct, one might expect to find the psycho-somatics somewhere between hysterics and dysthymics with a standard deviation larger than either.

The Neuroticism scale seems to be of much more certain value.

G. A. FOULDS

VOL. 5 1960/6

JEROME K. MYERS and BERTRAM H. ROBERTS: **Family and Class Dynamics in Mental Illness.** Chapman & Hall, London, 1959 295 pp., 56s.

THIS important book is the companion volume to HOLLINGSHEAD and REDLICH's 'Social Class and Mental Illness', and reports investigations into the bearing of social class differences upon the development, manifestation and treatment of two types of psychiatric illness. 25 schizophrenics and 25 neurotics between the ages of 22 and 44, and members of their families were intensively studied by a number of workers. The patients were almost equally distributed over HOLLINGSHEAD's social classes III and V, which are roughly equivalent with the small business and clerical class on the one hand, and the lowest unskilled labouring class, on the other.

The authors demonstrate that there are significant differences between the experiences of class III and class V patients in a number of areas—especially those of child-parent relationship, sexual development, pressures from the community, attitudes towards psychiatric illness and treatment, and symptomatology. Of special interest is the finding that stresses at each class level were found more frequently and with greater intensity among schizophrenic than among neurotic patients. Comparing patients with their siblings, upward social mobility or strivings towards it were associated with the development of psychiatric disorders in middle class patients, only—possibly because bottom class people rarely attempted to improve their position.

The investigators do not claim that social stresses, as found in their subjects, are the main cause of mental illness, but they demonstrate by numerous interesting instances the way in which stresses arising from some aspects of social class subculture or social mobility appear to push vulnerable personalities into serious breakdowns. There are full and non-doctrinaire discussions relating the results of the investigation to psychiatry in general, but some space might have been given to a complete, or at least abbreviated, presentation of the raw data obtained in one or two cases, and of the process in which various investigators extracted points for statistical analysis. Such a full presentation would have allayed one's lingering suspicion that some of the discovered characteristics and relationships had been due to the way in which the fieldworkers had obtained the raw data, or to unintentionally biased selection during their subsequent analysis.

FELIX POST

STELLA CHESS. **An Introduction to Child Psychiatry,** Grune and Stratton, New York and London, 1959, 254 pp., $5.25.

THERE has long been a need for an introductory book on Child Psychiatry for the use of psychiatrists training in adult work, paediatricians, general practitioners and others, who need to know something of this speciality. Dr. CHESS has set out to provide this for the American student and she has with advantage emphasised the close links that Child Psychiatry has with Paediatrics. The result is on the whole a clearly written book, well indexed and for those who wish to read further useful references to American writings. The complexities of the subject have not been avoided, although the author has had to be concise. Brevity, however, has its dangers; while some chapters could hardly be bettered, the subject matter in others and which concern common problems tend to be fragmented and may confuse the student. It is therefore surprising that so much space has been given up to Childhood Schizophrenia, which is relatively uncommon, and to a description of child analysis which is a rare event in the practice of Child Psychiatry. However, this is undoubtedly a useful book for the American student; it may be considered less serviceable to those working in other countries.

W. WARREN

J. M. VAN DER VALK: **Onderzoekingen over de electrische huidweerstand** (Researches on the electrical skin resistance.) Fix, Amsterdam, Antwerp. 1958, vii + 228 pp.

IN THIS book VAN DER VALK surveys the literature and describes the results of 10 years' research on 450 subjects (normals and patients with different internal diseases) as a member of the psychosomatic research team in Amsterdam. In his technic he used a 4·5 V battery and new silver electrodes, applied by a paste containing several electrolytes. Without neglecting the basic resistance values and the

psychogalvanic reflex, his study is especially concerned with the characteristics of the curve obtained by recording the resistance during a 10 min period in which the subject was first requested to sit still and be silent, then given a series of standard movement orders and questions provoking psychogalvanic responses. The findings may be summarised as follows. Smooth, straightly rising curves with high initial resistance and little psychogalvanic activity were found in subjects who controlled their emotions and in patients with coronary diseases, essential hypertension, peripheral vascular disease, diabetes and peptic ulcer. An often low starting, generally strongly declining curve, highly unsteady and with strong psychogalvanic activity was found in people who demonstrated their feelings more openly and in patients with neurocirculatory asthenia, ulcerative colitis, rheumatoid arthritis, gastritis, conditions with a high basal metabolism, functional diseases and pulmonary tuberculosis.

By different technical procedures (cutting of the current, reversing the current, changing the intensity of the current etc.) VAN DER VALK attempted to define the physical bases of the established data. He concludes that the curve is neither a consequence of potential differences on the skin, nor of polarisation, although it is influenced by the current applied. Measurements using two circuits with one common electrode demonstrate that the potential difference or resistance tended to decrease more under the cathode, whereas conversely an eventual increase of resistance occurred mainly under the anode. Thus during a rising curve the changes under the anode prevail, whereas in the course of a declining curve the changes under the cathode predominate. It is suggested that this results from the penetration of electrode paste into the sweat pores, which might be promoted or counteracted by the electric current. The amount of resistance is determined by the horny layer of the skin and the sweat pores and the different aspects of the curves can be explained mainly by changes in the moisture content of the sweat ducts. The psychogalvanic reflex appears in the same way under both the anode and the cathode and therefore must be due to a real change in resistance.

Concerning the physiological mechanisms regulating the phenomenon, the notable influence of sympathectomy, stellate ganglion injection and administration of a drug such as Banthine, as well as the finding that the curve obtained post mortem resembles the one found after sympathetic interruption are strong arguments suggesting that the sympathetic system exerts a regulating influence on the skin resistance. Simultaneous recording of skin temperature, finger plethysmogram, blood-pressure and pulse-frequency, together with experiments obstructing the circulation show that changes in skin resistance are not caused by changes in the circulation, although under certain circumstances the changes can occur simultaneously. There is a certain correlation between electrical skin resistance and the humidity of the volar surface of the hand.

This monograph is a thorough study of the clinical, physiological and physical aspects of the electrical skin resistance and its changes. At the same time it forms an ideal basis for those who wish to elaborate further the psychosomatic implications of psychological concepts such as the expression and control of emotions. By its methodological scientific approach it is a pioneer-work in the field of psychosomatic research and an English edition would certainly be welcome to all research-workers in this field.

R. A. PIERLOOT

Professor Dr. W. GRAB and Professor Dr. K. OBERDISSE: **Die medikamentose Behandlung der Schilddrüsenerkrankungen.** 55 Ab. Stuttgart: Thieme. DM 39.60. pp. 292.

THIS is a detailed and comprehensive exposition of the physiology of thyroid activity, its morbid variations and the clinical methods of investigating and treating thyroid disorder. Professor GRAB who is Director of the Pharmacological Institute in Giessen, is responsible for the first half of the book, which sets forth systematically the metabolic functions of the thyroid in health and disease and the general rationale of treatment by modern methods. The second part, by Professor OBERDISSE of Düsseldorf, is concerned with the treatment of individual disorders—hyperthyroidism, malignant exophthalmos, thyroiditis, carcinoma, goitre, and hypothyroidism. Both authors are well acquainted with English and American work, and their presentation does not differ substantially from that current in this country.

The authors accord very little space or interest to discussions of the psychological aspects of these disorders. They refer to the widespread belief that severe fright can provoke the advent of

VOL. 5 1960/6

hyperthyroidism, but they give reasons—such as the rarity of well attested cases and the lack of evidence that the recent war increased the frequency of the disease in bombed populations—for assuming that terror can only have this effect in specially constituted persons. In the converse process, whereby pathological changes in thyroid function bring about mental disturbances, they presume that these are mediated through metabolic effects on the ganglion-cells of the midbrain. Rather too confidently they maintain that the mental changes in hypothyroid conditions are wholly reversible: they dwell on the adult forms and give only scanty consideration to cretinism.

The book is well produced and documented; in spite of temptations to put in everything the clinician and the pathologist have to say about these conditions, the authors adhere admirably to their aim of presenting mainly the therapeutic aspects of thyroid disorder.

AUBREY LEWIS

P. H. CONNELL: **Amphetamine Psychosis.** (Maudsley Monograph No. 5). Chapman and Hall, London, 1960. 21s.

THIS is a monograph with which no clinician will quarrel. He need not be either a statistician or a fully trained biochemist to evaluate the text. The fact that the author was able to collect one of the largest series of cases of amphetamine psychosis in the world literature from four hospitals without undue difficulty will stimulate the interest of those who might otherwise be inclined to regard the condition as a rarity better left to workers at University Clinics and the like. Dr. CONNELL presents his material in a style that is quiet, confident and modest. Statements concerning the personality before illness of the patients may lack the elegance and sophistication of those who would only base their conclusions on batteries of personality tests, but they are made in such a way that there is no problem of communication for the clinician for whom this work is primarily intended. The author clearly defines his descriptive terms so that those of any school may understand.

He draws attention to an interesting and important point in this heyday of tranquillisers. It is not only insulin coma therapy that might be credited with dramatic cures in patients mistakenly labelled "schizophrenic", but any of the ataractics now available. Physicians alive to the possibility of amphetamine psychosis will be less likely to make this error.

The statement is frequently made that the previous personality of a patient may markedly influence the content of a psychiatric illness. Dr. CONNELL produces evidence to suggest that this is not so for those developing amphetamine psychosis, since patients with the kind of personality usually considered to predispose to paranoid illness were in the minority in his group. If this observation were confirmed and extended to other toxic and drug induced states, it might form a useful point of departure for the comparison of drug induced and the so-called "endogenous" psychosis in man.

It has not been previously emphasised that these drugs are true hallucinogens, nor has it been generally recognised either that single doses may produce psychotic reactions or that very considerable quantities may be absorbed by inhalation.

A biochemical test for urinary amines is carefully validated and a chromatographic technique for identification of the specific amine is described. He produces biochemical evidence that leaves the reader in no doubt (a) that inhalation of the drug can constitute a serious psychiatric hazard, and (b) that the test is within the range of any laboratory.

It is doubtful whether the author's recommendation that the methyl-orange test should be routinely used in all inpatient and outpatient mental hospital practice will be universally adopted. A large hospital with its outpatient clinics would soon tax any laboratory, even at the rate of 2 hr for each half-dozen tests. He might have been more realistic if he had confined his recommendations to anxiety states and paranoid schizophrenics.

This is a monograph that will be read with profit both by the general physician and the psychiatrist.

J. G. GIBSON

HANS SELYE: **The Chemical Prevention of Cardiac Necroses.** The Ronald Press Company, New York. ix + 235 pp.

PROFESSOR SELYE found that if rats are treated with normally innoxious amount of various corticords and at the same time receive certain sodium salts (NaH_2PO_4, Na_2SO_4 or $NaClO_4$) fatal cardiac necroses

may rapidly develop. These necrotic areas are usually in the right ventricle, the atria and the subendocardial layers of both ventricles. They are of a type first described by Fiedler (1899) under the title of "acute interstitial myocarditis" and concerning which a large amount of work has been carried out. Professor SELYE in his usual thorough and painstaking way, proceeded to analyse the conditions under which such lesions could be produced in his experimental animals. The result is a fascinating study of experimental pathology, in which the role of various corticoids, electrolytes, and physical and psychological agents is systematically investigated. The finding that KCl or $MgCl_2$ may protect the animal against the development of such lesions has obvious relevance to the problems of coronary thrombosis in man, although it is difficult to assess the significance of the findings in this regard. Although a critical evaluation of Professor SELYE's work demands a highly specialised knowledge which few but research workers in the field of cardiology possess, readers of this journal will anxiously await their verdict, and in any case will need to study the work for themselves. The book is a "must" for all of us who are concerned with psychosomatic medicine.

DENIS LEIGH

RENEE C. FOX: **Experiment Perilous: Physicians and Patients Facing the Unknown.** The Free Press, Glencoe, Illinois, 262 pp.

IN this book, RENEE FOX describes in some detail the results of a sociological study of a metabolic ward. The physicians on this ward were residents who had just entered the field of clinical investigation and were, therefore, wrestling with the problems posed by having multiple goals. As physicians they wished to give the best possible care to their patients; as investigators they wished to learn as much as possible from their experiments. Similarly, the patients who had volunteered to be hospitalized on this ward wished to be cured or improved in well-being, insofar as this could be achieved, and wished to contribute to science. When these goals could be attained simultaneously, both physicians and patients were enthusiastic, as this book attests. When these goals came into conflict with each other, stresses were imposed upon the individuals concerned and upon members of their groups. *Experiment Perilous* describes these stresses and the means utilized to meet them in a readable and enjoyable manner.

Though the author wished to focus primarily on interactions between physicians and patients, the reader misses a description of the part played by the nurses, dietitians, ward aides and laboratory technicians who also constitute a part of the social community. Neither does the author provide a discussion of the potential implications of the findings of this study for general sociological theory. She offers rather, an engaging story of young people caught in a web of psychological and social interactions in the environment of a research ward and she deals with them with definite warmth and understanding.

WILLIAM W. SCHOTTSTAEDT.

The Fifth Mental Measurements Year Book. Edited by OSCAR KRISEN BUROS. The Gryphon Press, New Jersey, xvii + 1292 pp., $22.50.

DEDICATED to Cyril Burt, this magnificent production covers a seven year period (1952–1958) of work in psychology. It attempts to list all the commercially available tests—psychological, educational and vocational, "published as separates in English-speaking countries", and all books on measurement published over the seven year period. There is a list of 957 tests, and these are critically reviewed by a galaxy of distinguished psychologists. 485 books on measurements and closely related fields are listed, and the Year Book, by printing a representative coverage of the reviews given to any particular book, tries to present a balanced view of the usefulness or otherwise of the book in question. The tests themselves run from "T.A.T. for African subjects" to "First Year Algebra: Every Pupil Scholarship Test", through every possible test known to clinicians such as the Rorschach, M.M.P.I. Wechsler-Bellevue, Cornell Index and so on. To say the book is a mine of information is almost an understatement; it is certainly essential for any research worker who is involved in psycho-somatic

VOL.
5
1960/6

research to have access to it. For the clinician, one of the most difficult tasks is to keep in touch with developments in psychology and it seems at times as if every psychologist has invented a test of his own. Our colleagues speak of tests, of the significance of which we are unsure; and many of us are quite ignorant of the tests employed in vocational guidance, in the field of education, and in various special fields. And yet the help a psychologist can give may be of the utmost importance for the subsequent life of our patients. A compendium such as this is an invaluable source of reference for the psychiatrist. For the psychologist, faced with a large and growing literature, some abstracting system is essential, and the fact that this is the fifth production in its line speaks for itself. This volume will join its predecessors on the reference shelves. The production, editorial work, typography and indexing is of the highest order and the book is not expensive.

DENIS LEIGH

Angst und Schuld in theologischer und psychotherapeutischer Sicht. (Anxiety and Guilt from the Theological and Psychotherapeutic Point of View). Edited by W. BITTER. Ernst KlettVerlag, Stuttgart, 1959. pp. 186.

THIS is a collection of papers presented to a conference of medical psychotherapists and ministers of religion. The aim of the conference was the clarification of their respective attitudes towards fear and guilt which are of common concern to both groups. They agreed that although the theological and psychological approaches to those sentiments were fundamentally different, they were not incompatible. It was essential for the psychotherapist to understand the religious attitude to fear and guilt and for the minister of religion to be familiar with the psychological approach. They had to respect each other's territory. A book like this should help to dispel mutual distrust and misconceptions

E. STENGEL.

VOL.
5
1960/6

Journal of Psychosomatic Research, 1961, Vol. 5, pp. 73 to 82. Pergamon Press Ltd. Printed in Northern Ireland

ALTERATIONS IN PHYSIOLOGICAL MEASURES DURING EXPERIMENTALLY INDUCED ATTITUDES*†

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IN A previous paper (GRAHAM, STERN and WINOKUR, 1958), the authors reported an experiment in which subjects were told, under hypnosis, to assume one or the other of two attitudes. It was predicted and confirmed that skin temperature would rise with one of the attitudes and fall with the other. The present study was an attempt to reproduce these results under special conditions and to extend the method to a third attitude and to other physiological variables.

The purpose of this and the previous study was to test experimentally a specificity of attitude hypothesis proposed by GRACE and GRAHAM (1952). From interviews with 128 patients having 11 psychosomatic diseases or symptoms, these authors suggested that there was associated with each disease a specific attitude towards a life event occurring at the onset or before an exacerbation of the disease. A similar specificity hypothesis has been advanced by ALEXANDER (1950) and others. The major difference in the present approach is that the symptom is said to be primarily related, not to a nuclear conflict nor to a personality characteristic, but to the way an individual perceives, and what he wants to do about, a precipitating event. Since basic conflicts and personality configurations undoubtedly affect an individual's perceptions and motives, a correlation might also be expected between symptoms and any major personality variable. However, it is likely that the extent of the relationship between a psychological variable and a physiological variable will decrease when the variables are separated in time in the life history of the individual.

The specificity hypothesis not only advanced the general proposition of specific attitudes associated with specific symptoms, but, for the 11 symptoms investigated clinically, elaborated the attitudes and the kind and direction of physiological changes which should be associated. An attitude was defined as (1) how a person perceives his own position in a situation—what he feels is happening to him—and (2) what action, if any, he wishes to take. A test of the predictions requires, then, production of an attitude and measurement of the appropriate physiological variable.

The general technique employed in this and the previous experiment was to suggest attitudes directly to a subject under hypnosis. The attitude, in such a case, is defined by the operations of the experimenter and requires no inferences as to what the subject does or does not feel. This method has the advantage, rare in this field, of putting the independent variable under experimental control. It should be noted that there was no interest in investigating hypnosis itself. It was used only as a technical aid in controlling the subjects' attitudes and in reducing environmental distractions.

In the first study (GRAHAM, STERN and WINOKUR, 1958), two attitudes were suggested, one previously found to be associated with hives and one found to be associated with Raynaud's disease. Since warming of the skin is part of the physiology of hives (GRAHAM, 1950), while cooling is characteristic of Raynaud's disease, these two attitudes should lead to sharp physiological distinction. Results confirmed the predictions. It was also shown that alternative explanations in terms of a tendency for

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temperatures (a) to continue a trend already begun, (b) to reverse a trend, or (c) to approach some hypothetical (optimal) value could not account for the results. There was a definite tendency to continue a trend, but this trend was successfully overcome by the attitude suggestions when the two factors were opposed and was increased when they were in accord.

In the present experiment, an attempt was made to replicate the results of the first experiment under relatively unfavorable conditions—that is, to determine whether attitude suggestions could successfully reverse strong trends in the opposed direction. This would require the hives attitude to reverse a falling temperature trend and the Raynaud's attitude to reverse a rising temperature trend. A third attitude, that associated with essential hypertension, was also suggested. Since the special hallmark of the disease, essential hypertension, is an increase in diastolic blood pressure, this physiological variable was also measured in the present experiment. In addition, three "neutral" physiological variables, systolic blood pressure, pulse rate and respiratory rate, were included. No predictions were made concerning differential changes in these. There were thus three independent variables, the three attitude suggestions, and five dependent physiological variables. Each attitude was compared with each of the other two attitudes for the direction and relative extent of change in the five physiological variables. Fifteen comparisons were thus involved, for five of which specific predictions were made. It was predicted that the skin temperature would fall with the Raynaud's attitude and rise with the hives attitude and that the change with hypertension should be less than either of these. It was also predicted that the diastolic blood pressure would show a greater rise with the hypertension attitude than with either of the other two attitudes.

VOL.
5
1960/6

PROCEDURE

Subjects. As in the first study, subjects were healthy young male volunteers, who were undergraduates either in college or at a theological seminary. They were screened to eliminate any with serious emotional disturbance and were paid for taking part in the experiment. The age range was from 18 to 26. A total of 45 hypnotic sessions were conducted with 22 subjects. Of these, 17 sessions were excluded because of pronounced cooling in the preliminary control period. Reasons for excluding sessions in which there is a marked vasoconstrictive tendency were discussed in the first paper (GRAHAM, STERN and WINOKUR, 1958) and criteria for determining whether or not cooling occurred were specified. These were: (1) a drop in skin temperature of more than 1·5°C between the time the subject entered the laboratory and the induction of the first attitude, or (2) a drop of skin temperature to 30·0°C or less during the same period. The number of sessions remaining for analysis was 28 and involved 18 subjects.

Apparatus. Experiments were conducted in an air-conditioned laboratory with a variation in room temperature of not more than 1·5°C during any one session. The subject was seated in an adjustable lounge chair which permitted him to lean back and relax comfortably. Skin temperature was measured by means of a thermistor taped to the dorsum of the left hand, connected to a galvanometer which permitted readings to 0·01°C. Readings were made at 1-min intervals. Electrocardiographic leads were applied to the right arm and left leg. A thin metal strip attached to a strain gauge and resting on the subject's sternum permitted counting the respiratory rate. This was not technically very satisfactory, however, since movements of the subject sometimes dislodged the metal strip, and some of the respiratory records are therefore incomplete. Both the electrocardiogram and the respiratory rate were recorded continuously on a polygraph. The arterial blood pressure was obtained by use of an automatically recording sphygmomanometer which responds to sound signals over the brachial artery. This instrumentation made it unnecessary to touch the subject during the experiment. Only three blood pressure measurements were made during each 10-min period since it was felt that more frequent determinations ran the risk of producing vascular congestion in the arm, with consequent interference with the production of the blood pressure sounds.

Method. The procedure was to attach apparatus necessary for recording of physiological changes to the subject at the beginning of a session. After a period of time sufficient to allow the skin temperature of the hand to reach a state of relative stability, the subject was hypnotized by the method of ocular fixation. Several methods for testing the depth of the trance state were employed. When hypnosis had been achieved, the subject was told to relax and physiological variables were recorded for a 10 min control period. The subject was then given an attitude suggestion for 10 min. This was the first experimental attitude period. The subject was told once again to relax for a 10–min control period and this was followed by a second experimental attitude period during which a different attitude suggestion was given for 10–min. Another period of relaxation was induced, followed by awakening and a period of reassurance and discussion with the subject of as much of the experiment as he remembered. The entire experimental session lasted approximately 2 hr.

The Raynaud's attitude was suggested 26 times, the hives attitude 11 times and the hypertension attitude 27 times in the 28 sessions included in the study. Hypertension and Raynaud's suggestions were made with greater frequency because the hypertension suggestion was being employed for the first time and because it was expected that it would be more difficult to differentiate hypertension from Raynaud's than from hives. Every session, with one exception, included two attitudes, with the orders of presentation approximately equalized over the series. When the initial stabilization period was not prolonged, it was possible to suggest a third attitude also.

The method used to induce the hives and Raynaud's attitudes was the one employed in the majority of the sessions of the first experiment. The subject was touched with an unlighted match on one hand, *not* the one to which the thermistor was taped. The suggestion given for the hives attitude was as follows: "Dr. X is now going to burn your hand with a match. When he does so you will feel very much mistreated, very unfairly treated, but you will be unable to do anything about it. You can't even think of anything you want to do about it, you just have to take it. You are thinking only of what has happened *to* you". For the Raynaud's attitude the procedure was the same except that the subject was told "you feel mistreated and you want to hit Dr. X. You want to hit him just as hard as you can, you want to hit him and choke him and strangle him. That's all you're thinking about, how much you want to hit him". The hypertension suggestion was as follows: "Dr. X is going to burn you or shock you or do something else to you that may be painful. It may injure you, it may even be dangerous. You have to be ready for whatever he's going to do, you have to be alert and on guard and try to be prepared. You just have to wait for something that may be painful and dangerous, you can't prevent it. You feel you are in danger and you have to watch out, to be ready for anything." In all cases, continual reinforcement of the attitude was given throughout the 10–min period by repetition of phrases from the instructions. Three of the authors served as experimenters, two of them being present throughout each session. Each experimenter acted as hypnotist in approximately one third of the experiments.

Treatment of data. As in the first experiment, the data subjected to analysis were the ten readings at 2–min intervals during the attitude period and the preceding control period, except in the case of blood pressure where only three readings were obtained in each of the periods. The reading 1 min before attitude suggestions were begun, that is, the last control reading, was taken as the reference point for computing changes. Readings before and after this point were recorded as rises or falls in degrees of temperature, ml of blood pressure and so on. The absolute gain or loss was used since scatter graphs indicated that the lines of regression closely

approximated a slope of 1·0, and little improvement in accuracy would be gained by correcting for the exact regression. Use of ratios or of relative change would clearly distort the data. LACEY (1956) has discussed this problem at considerable length. Changes were computed separately for each subject so that in determining the change from control to attitude period each subject served as his own control.

In addition to the absolute rise or fall, the average rate of change per minute (or slope of the best-fitting line) was computed for the control period and, in the case of temperature, for the first 4 min and the last 6 min of the attitude period. In order to use all of the recorded data, per min rate of change was computed by averaging the slope of the lines passing through each of the points and the reference point. These were calculated separately for each subject.

TABLE 1.—LAST CONTROL READINGS (MEANS AND STANDARD DEVIATIONS)

	Hives	Raynaud's	Hypertension
N	11	26	27
Skin Temperature (°C)	33·7 ± 1·08	33·5 ± 1·01	33·2 ± 1·57
Diastolic Pressure (mm Hg)	79·9 ± 9·53	79·6 ± 10·43	78·2 ± 10·42
Systolic Pressure (mm Hg)	124·6 ± 14·86	123·6 ± 16.68	123·2 ± 16·65
Heart Rate (beats/min)	74·1 ± 12·15	77·2 ± 13·68	75·8 ± 16·66
Respirations/min*	16·7 ± 3·86	15·8 ± 2·94	16·2 ± 3·34

* Due to methodological difficulties, respiration readings were not available on some Subjects. The exact *N*'s are: Hives—9, Raynaud's—18, Hypertension—17.

TABLE 2.—RATES OF CHANGE PER MIN DURING THE CONTROL PERIOD (MEANS AND STANDARD DEVIATIONS)

	Hives	Raynaud's	Hypertension
N	11	26	27
Skin Temperature (°C)	−0·03 ± 0·028	+0·06 ± 0·055	+0·03 ± 0·052
Diastolic Pressure (mm Hg)	−0·48 ± 1·741	−0·15 ± 1·670	−0·79 ± 2·148
Systolic Pressure (mm Hg)	+0·34 ± 4·889	−0·20 ± 2·582	−0·52 ± 1·725
Heart Rate (beats/min)	−0·07 ± 1·621	−0·40 ± 1·026	−0·58 ± 1·086
Respirations/min*	−0·04 ± 0·556	+0·16 ± 0·696	−0·07 ± 0·907

* Due to methodological difficulties, respiration readings were not available on some Subjects. The exact *N*'s are: Hives—9, Raynaud's—18, Hypertension—17.

RESULTS

Control period comparisons

Tables 1 and 2 show, respectively, the mean value of the last control reading and the mean rate of change per min during the control period on each of the five physiological variables for each of the attitude groups. There were no significant differences between groups at the time of the last control reading and, except for temperature, there were no significant differences in the rates of change per minute of any of the physiological variables during the control period. As previously noted, in the case of temperature, an effort was made to introduce the hives attitude when the temperature was falling and to introduce the Raynaud's attitude suggestions when the temperature was rising.

VOL.
5
1960/6

Attitude period comparisons (DBP, SBP, pulse, respiration).

Temperature will be considered separately since the need to equate for differences in rate of change during the control period requires different statistical treatment. Results for diastolic blood pressure (DBP), systolic blood pressure (SBP), pulse rate, and respiratory rate are given in Table 3. All variables rose during the attitude period and, as the table indicates, in a number of cases the rise represented a significant change from the last control reading. As noted above, the average change is based on three attitude readings for the blood pressure data and on five attitude readings for pulse and respiratory rates. Both the average change and the maximum rise have

TABLE 3.—AVERAGE CHANGE AND MAXIMUM RISE DURING THE ATTITUDE PERIOD (MEANS)

	Hives	Raynaud's	Hypertension
N	11	27	26
Diastolic Pressure (mm Hg)			
Average	+0·30	+2·94†	+3·17*
Maximum	+3·91	+6·81†	+8·48†
Systolic Pressure (mm Hg)			
Average	+2·33	+3·82*	+2·00
Maximum	+7·54	+9·42†	+6·30†
Heart Rate (beats/min)			
Average	+4·25	+8·06†	+6·44†
Maximum	+8·27*	+12·16†	+10·83†
Respirations/min‡			
Average	+2·37	+4·54	+4·70
Maximum	+6·00	+8·22	+7·92

* $P = 0{\cdot}05$
† $P = 0{\cdot}01$
‡ Due to methodological difficulties, respiration readings were not available on some Subjects. The exact *N*'s are: Hives—9, Raynaud's—18, Hypertension—17.

been computed since maximum or minimum values have frequently been preferred to averages in the analysis of physiological data. (AX, 1953; SCHACHTER, 1957).

Absolute changes, whether measured by the average change or by the maximum change method are of less interest for the purposes of the present experiment than a comparison of the relative change in the different attitudes. These were evaluated by determining whether the change under one attitude was more or less of a rise than that under another attitude given to the same subject during the same session. Each subject thus served as his own control. The results of the comparisons are shown in Table 4. The only prediction made by the specificity hypothesis was that the hypertension attitude would produce an increase in diastolic blood pressure. While no prediction was made concerning diastolic changes under hives and Raynaud's attitudes, the essential point of the theory is that whatever the direction or amount of change with other attitudes, there should be less increase than that seen with the hypertension attitude. Diastolic blood pressure may rise with many diseases but it is in the disease, essential hypertension, that the rise becomes of major consequence.

Table 4 shows that the rise in DBP was significantly greater with the hypertension attitude than with the hives attitude but not significantly more than with the Raynaud's

attitude. No predictions concerning differences in the other physiological variables were made and, with the exception of a significantly greater average DBP rise in Raynaud's than in hives, no significant differences were obtained.

TABLE 4.—*t*-RATIOS OF DIFFERENCES IN PHYSIOLOGICAL CHANGES UNDER THREE ATTITUDE SUGGESTIONS

	Hypertension > Hives	Hypertension > Raynaud's	Raynaud's Hives
Paired *N*	10	25	10
Diastolic Pressure (mm Hg)			
Average change	2·06*	0·01	3·09†
Maximum change	2·13*	0·96	1·75
Systolic Pressure (mm Hg)			
Average change	0·06	0·96	0·10
Maximum change	0·05	1·59	0·14
Heart Rate (beats/min)			
Average change	0·57	0·61	0·72
Maximum change	0·53	0·08	0·11
Respirations/min‡			
Average change	—	0·01	0·03
Maximum change	—	0·10	0·12

* $P < 0{\cdot}05$ in a one-tailed test
† $P < 0{\cdot}01$ in a one-tailed test
‡ The *N* available for paired comparisons of respiration were, in order, 6, 16 and 8.

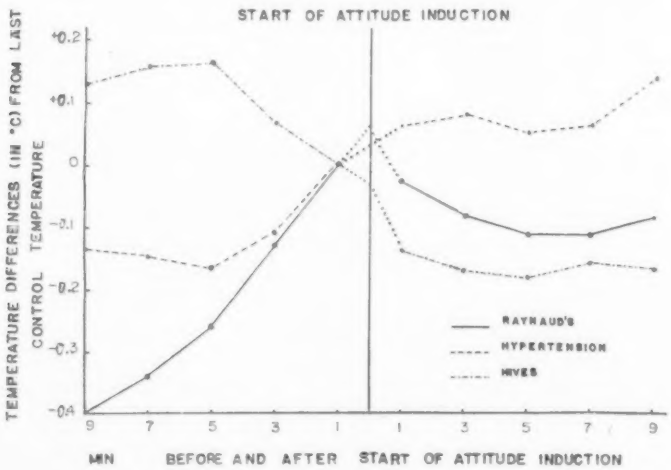

FIG. 1. Mean difference between hand temperatures at the last control reading and at the other times indicated.

Attitude period comparisons (temperature)

Temperature changes during the control and attitude periods are plotted in Fig. 1 for the three attitude groups. Lines between the last control readings and the first attitude readings, which were 1 min before and 1 min after introduction of the attitude, have been dotted since these two points were not connected by a straight

line but are extrapolations of the preceding and following slopes. This was done to emphasize the point that introduction of any attitude suggestion led to an initial fall or deceleration. The phenomenon was also observed in the first experiment (GRAHAM, STERN and WINOKUR, 1958) and was thought to be best explained as a "startle" response to the "phantom burn" or to a new stimulus.

Following this initial deceleration in response to the attitude suggestion, the hypertension attitude group tended to resume its rise while the Raynaud's attitude

TABLE 5.—MEAN CHANGE IN SLOPE OF THE TEMPERATURE CURVE DURING THE ATTITUDE PERIOD

		Initial	Last
	N	4 min	6 min
Hives			
Experiment I	23	−0·024†	+0·038
Experiment II	11	−0·023	+0·028*
Raynaud's			
Experiment I	18	−0·056†	−0·066†
Experiment II	26	−0·081†	−0·072†
Hypertension			
Experiment II	27	−0·004	−0·031

* $P < 0{\cdot}05$
† $P < 0{\cdot}01$

group remained below the last control temperature throughout the attitude period although it had previously shown a marked rising trend. In contrast, the hives group, previously falling, began to rise. However, temperatures did not rise above the last control reading at any time. The attempt to produce an absolute rise in hives in opposition to a falling trend during the control period was obviously unsuccessful.

While absolute rises and falls did not conform to predictions, the graph does show a reversal in the slope of the temperature curve, both for hives and Raynaud's groups, in the direction predicted by the hypothesis. That is, when differences in the slope during the control periods are equated, the change in the attitude period is in accord with expectation. The mean changes in slope (or rate of change per min) are shown in Table 5 for the three groups in the present experiment and for the two groups employed in the previous experiment. In order to reduce the effect of the initial "startle", the slopes were calculated separately for the first 4 min of the attitude period and for the last 6 min, that is, from the last control reading to the 3-min attitude reading and from the 3-min attitude reading to the 9-min attitude reading. Inspection of temperature curves obtained in the first experiment suggested that, with readings at two min intervals, an inflection of the curves was most likely to occur at the 3-min point.

It can be observed from Table 5 that results in the two experiments are similar. In both experiments, the initial deceleration was greater with Raynaud's than with hives and, in both experiments, the hives attitude group showed a relative acceleration of the temperature slope and the Raynaud's attitude group a relative deceleration during the last 6 min of the period. The hypertension group showed less deceleration

in its initial response to introduction of the attitude suggestion than did the other groups. During the last 6 min, there was continued deceleration in the hypertension group but it was less marked than with the Raynaud's attitude.

t-Tests of the significance of these differences between attitude groups are shown in Table 6 for the change in slope during the last 6 min of the attitude period. Differences during the first 4 min are not compared, on the assumption that the initial reaction to the attitude suggestion was primarily a "startle" effect which is relatively

TABLE 6.—*t*-RATIOS OF DIFFERENCES IN TEMPERATURE SLOPE CHANGE UNDER THREE ATTITUDE SUGGESTIONS (WHOLE CONTROL VS. LAST 6 MIN OF ATTITUDE)

	Unpaired Total groups	Paired Subjects
Different attitudes		
Hives vs Raynaud's, Exp. I	3·92†	
Hives vs Raynaud's, Exp. II	3·19†	3·68†
Hives vs Hypertension, Exp. II	2·08*	2·33*
Raynaud's vs Hypertension, Exp. II	1·61	1·60
Same attitudes		
Hives, Exp. I vs Hives, Exp. II	0·38	
Raynaud's, Exp. I vs Raynaud's, Exp. II	0·21	

* $P < 0{\cdot}05$ in a one-tailed test
† $P < 0{\cdot}01$ in a one-tailed test

undifferentiated. While this assumption is based on empirical findings and was not predicted on theoretical grounds, the empirical basis derives from the earlier study rather than the present one. Table 6 shows that the slope difference in the hives and Raynaud's groups is a significant one in both experiments while there is no difference in like-attitude groups in the two experiments. The slope change in the hypertension group lay between those in the hives and Raynaud's group. It was significantly different from the former but not from the latter. Table 6 also gives the *t*-ratios when paired comparisons of subjects given two attitudes in the same session were made. As would be expected, removing the variance associated with the subject and session differences increases the size of the *t*-ratios.

DISCUSSION

In the present experiment, three attitudes were suggested to Subjects and each attitude was compared with each of the other two attitudes for direction and relative extent of change in 5 physiological variables. On the basis of a previously published hypothesis concerning specificity of attitude, predictions were made as to changes that should occur in 5 of the 15 possible comparisons. No predictions were made concerning the 10 remaining comparisons. One of these could not be completed because of technical difficulties in recording some of the respiratory rate data. Only one of the other 9 *t*-tests showed a significant difference between attitudes and this was true with only one of 2 measures of change. In contrast, of the 5 comparisons for which predictions were made, 3 were confirmed. The other 2 were in the predicted direction. It should be emphasized that each of the 5 predictions specified direction so that each could have been rejected had significant differences in the opposed direction been obtained.

VOL.
5
1960/6

The value of these findings as a demonstration of the utility of the specificity of attitude hypothesis depends in part on the availability of alternative explanations of the results. It is difficult to see how these differential changes could be predicted by either a theory emphasizing uniformity of response to "stress" or by one emphasizing individual reaction patterns. Some attention has been given recently to the idea that there are situation or stress-specific factors and a few experiments have emphasized that the pattern of physiological change is different in different affective states. However, such studies have been concerned simply with demonstrating that there are differences and have not formulated any but a *post-facto* basis for predicting what the differences should be. The motor preparatory theory advanced by BULL (1945) is an exception to this.

It would go beyond the purposes of the present paper to expand this discussion into an evaluation of the relative merits of various theories of emotion or of psychosomatic disease. It is sufficient to indicate that the present results might be compatible with other approaches but would be difficult to predict from them.

Some comment should be made on the general method employed in this and the previous experiment. The independent variable in which we were interested was an attitude, defined as (1) what a person feels is happening to him and (2) what he wants to do about it. To produce specified attitudes in human subjects certainly presents a major difficulty. It was felt that introduction of specific stress situations would probably not be satisfactory. While Subjects might react "emotionally", they could show wide variability in the specific attitudes with which we were concerned. Direct suggestion of an attitude to a hypnotized subject was therefore attempted. This provided a means of manipulating the independent variable but whether or not it would prove a sufficiently strong stimulus might be questioned. The results of the two experiments suggest that the stimulus is strong enough to produce the differential changes in physiological variables with which we were concerned. It would be worthwhile to know how these changes compare in size with those obtained in various types of stress situation and to determine if direct suggestion without hypnosis might prove equally effective.

Another methodological point to be considered is whether or not anything would be gained by asking subjects after the hypnotic session if they had, in fact, experienced the attitudes suggested to them. Such a procedure might well lead to better confirmation of the specificity hypothesis, by excluding subjects who had not in fact adopted the attitudes suggested. It would, however, lead to obvious difficulties in scoring subjects' answers, and would in some ways, therefore, hardly represent an improvement over the original clinical findings which led to the present experiment. In fact, it appears that one strength of the present and previous (GRAHAM, STERN and WINOKUR, 1958) studies, is that verbalizations of the subject need *not* be taken into account.

Finally, it should be emphasized that these first two experiments necessarily have been to some extent exploratory. Many technical problems had to be resolved by arbitrary decisions. How long a control period is necessary to provide stability of measures? How long can an attitude suggestion be sustained without encountering fatigue, adaptation or similar effects? What is the best method to use in inducing an attitude? What depth of hypnosis should be employed? A number of such questions could be answered by experimentation but it seemed more efficient to determine

whether or not the general method was workable before proceeding to answer technical questions. Since the method does appear workable and, indeed, is potentially a means for manipulating a wide variety of psychological variables, future work will be directed to technical problems as well as to testing other predictions of the theory.

SUMMARY

Young, healthy subjects were told, under hypnosis, to assume one or another of three attitudes. The attitude suggestions instructed the subject how he should perceive his own position and what action, if any, he wished to take. The three attitudes were those found in a previous clinical study to be associated with hives, Raynaud's disease, and essential hypertension. The hypothesis to be tested was that the physiological changes characteristic of these diseases would occur when the attitudes associated with them were suggested. Specifically, diastolic blood pressure should rise under the hypertension attitude, skin temperature should rise with the hives attitude and skin temperature should fall with Raynaud's attitude. Systolic blood pressure, pulse rate and respiration rate were also recorded but no predictions were made concerning changes in these variables.

Results supported the hypothesis in part:

(1) With the hypertension attitude, there was a rise in diastolic blood pressure which was greater than the rise with the Raynaud's attitude and significantly greater than the rise with the hives attitude.

(2) During the first 4 min of the attitude period, there was a drop in skin temperature with all attitudes. This initial "startle" effect was also observed in a previous experiment.

(3) During the last 6 min of the attitude period, the skin temperature rose with the hives attitude and remained stable with the Raynaud's attitude. When significant differences in the slopes of the temperature curves during the control period were equated, changes in slope during the attitude period differed in accord with expectation. Results with the hives and Raynaud's attitudes were significantly different and replicated findings of a previous experiment. The change under the hypertension attitude fell between the hives and Raynaud's attitude slopes and was significantly different from the hives but not from the Raynaud's results.

(4) There were no significant differences among attitudes in systolic blood pressure, pulse rate or respiration rate.

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ALLERGY AND NEUROSIS IN ASTHMA*†

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INTRODUCTION

ALTHOUGH different etiological factors have been considered bronchial asthma remains an entity of unknown origin. The role of infectious, allergic, psychological, social, endocrine and hereditary factors has recently been discussed (GROEN, ORIE, JONXIS, HUËT, SCHOOK, BASTIAANS and DOELEMAN, 1957). Several attempts have been made to classify asthma patients according to the etiological factor which was considered to be of primary importance (NOELPP and NOELPP-ESCHENHAGEN, 1956). Some authors thus distinguish patients with psychogenic asthma from those with allergic asthma (FRENCH and ALEXANDER, 1941; HANSE, 1934; RACKEMANN, 1950; STRAUSS, 1927; WYSS, 1955; WITTKOWER and PETOW, 1952; ZIEGLER and ELLIOT, 1926). Such a distinction is only valuable if it can be shown that there is a negative correlation between allergological and psychological factors in the etiology of the disease in these patients. The few investigations dealing with the correlation of these factors have produced conflicting results.

MCDERMOTT and COBB (1939) found emotional factors to be active in 37 out of 50 asthma patients. These could not be demonstrated in the remaining group of 13 patients. These authors found no clear difference in the frequency of positive skin-reactions in these two groups.

HARRIS, RAPOPORT and RYNERSON (1950) compared two groups of asthmatic children. In one group psychic factors were considered to be of primary importance. Contrary to their expectation they found no difference in the therapeutic results of allergic desensitization between this group and a second group in which emotional factors were not considered to be important.

DEKKER and GROEN (1956) and DEKKER, PELSER and GROEN (1957) were able to provoke attacks of asthma in the laboratory in some patients both with allergic and with psychic stimuli. They concluded that there is a category of asthma patients in which both factors may contribute. MITCHELL, CURRAN and MEYERS (1947) classified 1129 asthma patients according to the predominant etiological factor. They obtained the following results: allergy 49·5 per cent‡, recurring bronchitis 14·5 per cent, emphysema 5·6 per cent, other 6·6 per cent. There remained a group of 22·7 per cent in which no etiological factor could be found. The results of anti-allergic treatment in the allergic patients were described as "highly successful". This treatment failed in the non-allergic patients. This classification was then repeated in a second group of 100 asthma patients but now attention was also focused on psychological factors. The distribution over the different groups was very similar but now they found personal maladjustment in the group of 21 patients in whom no casual somatic disturbance had been found. This finding suggests a very strong negative correlation between allergic and psychic factors. No mention was made however of any psychological investigation in those patients in whom a somatic etiology was assumed and there are no data about the percentage of "normal" individuals satisfying the criteria for "personal maladjustment" used in this study.

REES (1956a) examined a group of 441 asthma patients, male and female from 0–65 years. This investigator came to the conclusion that psychological factors were the only cause in 18 per cent, allergic factors in 4 per cent and infectious factors in 17 per cent in these cases. In the majority of his patients (61 per cent) several factors were operative simultaneously, but in these patients he also

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‡ Corrected by the authors

gave a classification according to the predominant etiology. Later on several other groups of asthma patients have been classified according to the same criteria (REES, 1956b; WILLIAMS, 1958).

The classification of the asthma patients along these lines has up to now been greatly asthma-dependent on the subjective judgement of the investigator or on a compromise between investigators from different disciplines weighing their respective findings in the same patients. The estimation of the allergological aspects have been dependent on the history and skintesting and on the results of antiallergic treatment. The psychiatric judgement has been based on the results of interviews in some cases supported by projection tests such as the Rorschach-method.

The significance of positive skin tests is controversial (TEN CATE, 1954; BASTIAANS and GROEN, 1954; GROEN, ORIE, JONXIS, HUËT, SCHOOK, BASTIAANS and DOELEMAN, 1957; HERXHEIMER, 1952; OGILVIE, 1954) and the combined interpretation of positive skin tests and history and the judgement about the efficacy of antiallergic treatment introduces an important subjective element. The same can be said about the interpretation of projection tests and the psychiatric interview (v.d. GIESSEN, 1957). We were unable to find a comparative investigation of psychological and allergological factors in asthma patients by objective means. This paper deals with two such investigations in two towns in different parts of the country, testing the hypothesis, that there is a negative correlation between allergological and psychological etiological factors in asthma patients.

CASE MATERIAL

All patients were females. The first part of the investigation was carried out in the Wilhelmina-Gasthuis in Amsterdam in 39 female asthma patients between the ages of 26 and 55 years (mean, 40 years; S.D., 8·4).

In order to minimize the risk of irrelevant factors influencing our results such as selection of patients on the basis of our interest in psychosomatic aspects, a similar investigation was done in the University Department for Pulmonary Diseases in Groningen, where the allergological approach is particularly stressed. Here 40 female asthma patients were examined between the ages of 21—45 years (mean, 37·5 years; S.D., 6·7). In all patients the diagnosis bronchial asthma was made after thorough examination in one hospital or in the outpatient department. Both groups were divided in a subgroup showing manifest allergy and a subgroup showing no manifest allergy. The neuroticism scores of all patients were obtained. The allergological and psychological investigations were done by independent observers who at the time of recording their results had no knowledge about the results obtained in the other field.

METHOD

Objective classification of patients with predominant psychologic or allergologic asthma calls for clear and objective criteria for the estimation of psychological and allergological factors. This was attempted in the following way:

(a) *Allergological investigations:*

Inhalation tests were done using the method described by LOWELL and SCHILLER (1947) in the modification of TEN CATE and ORIE (1953). In this method the patient inhales an aerosol of allergen solution. Its effect is observed clinically and registered by means of determinations of the vital capacity which are repeated every 4 min. The reaction was considered positive if the vital capacity decreased gradually over more than 10 per cent of the mean of the baseline values. According to TEN CATE (1954) no positive inhalation reaction will be observed with allergen extracts that gave

negative skin reactions if proper test concentrations are used. However, only a minority of positive skin tests corresponds to a positive inhalation test.

Unless an inhalant is capable of producing a positive inhalation reaction in a patient it cannot probably be considered as a causative agent. Skin reactions have only limited value in this regard. They can however be used as a screening procedure in order to determine which substance should be more thoroughly investigated. It was used as such in all our patients. The following allergen extracts were used: grass pollen, tree pollen, hay dust, house dust, moulds, feathers, kapok, animal hairs and incidentally some substances were used which appeared as possible offenders in the patients history. Together they formed a selection of those allergens which are commonly believed to be responsible for a majority of the attacks of asthma.

For the purpose of this investigation allergic factors were considered to be important in a particular patient if inhalation-tests of one or more allergens were positive. Allergological factors were considered to be unimportant if either all skin tests were negative or if all positive skin tests had been followed by a negative inhalation test for the particular allergen.

(b) *Psychological investigation:*

In the psychosomatic literature, asthma patients have been described as neurotics (FEDERN, 1913 GROEN, VAN DER HORST, BASTIAANS, GREWEL, VAN DER VALK and VLES, 1951; MCDERMOTT and COBB, 1939; SADGER, 1911; SAINSBURY, 1959; SCHATIA, 1941; WULFF, 1913).

It might be objected that this is a rather vague entity. From the work of EYSENCK (1952), however, resulted the concept that it is possible to use the degree of neurosis as a fruitful parameter regardless of its essence. EYSENCK (1952) introduced objective test methods by which the degree of "neuroticism" can be quantitatively expressed. This is similar to the way in which an estimation of "intelligence" is obtained by measuring the intelligence quotient. The reliability and validity of one of these tests i.e. the "Two Part Personality Inventory" has been described by HERON (1955). This test consists of a query asking 110 questions which must be answered by "Yes" or "No". Forty-two of these questions have a high loading for neuroticism. The "neuroticism score" consists of the number of questions answered in the neurotic direction. So this score may vary between 0 and 42.

BARENDREGT (1958) carried out a validation study with a Dutch version of this test in a group of normal individuals and in a group of neurotics. The normal subjects were selected to meet the following arbitrary criteria:

they were: (a) normally taking part in the production process
(b) never condemned in court
(c) never treated for a chronic disease
(d) never treated by a psychiatrist.

A group of patients seeking aid from the Amsterdam Psychoanalytical Institute for psychical complaints were considered to be neurotic. The mean neuroticism score in the normal group was 6·5 (S.D., 6) versus 18 (S.D., 6) in the neurotic group. It could be concluded that this version of the test also distinguishes with great reliability between these two groups of subjects from a Dutch population. Therefore the Two Part Personality Inventory was chosen as the objective criterion for the degree of neurosis in both groups of asthma patients.

DEFINITION OF PROBLEM

On the basis of the above considerations, our problem was re-defined as follows: is the neuroticism score lower in a group of asthma patients with a positive inhalation test than in a group of asthma patients in whom such positive inhalation tests could not be obtained? If this question should be answered in the affirmative then the distinction between allergogenic versus psychogenic asthma seems fruitful. If answered in the negative it must mean that the hypothesis that this distinction can be made, is in need of better support than is at present available.

RESULTS

These are summarized in Table 1.

It is evident from these figures, that there is no significant difference between the neuroticism scores of the "allergic" and the "non-allergic" asthma patients.

TABLE 1.—NEUROTICISM SCORES IN "ALLERGIC" AND "NON-ALLERGIC" ASTHMA PATIENTS

	Total number of patients	Manifest allergy			*P* values	No manifest allergy		
		N	Scores	S.D.		*N*	Scores	S.D.
1st investigation	39	18	**18·7**	5·5	0·78	21	**20·8**	6·6
2nd investigation	40	16	**18·2**	6·2	0·70	24	**16·4**	7·9
Combined results	79	34	**18·5**	5·9	0·85	45	**18·5**	7·5

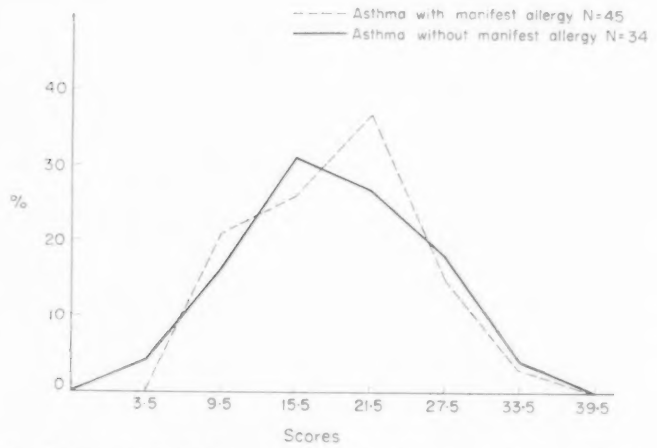

FIG. 1.—Frequency distribution of the neuroticism scores in the "allergic" and the "non-allergic" groups.

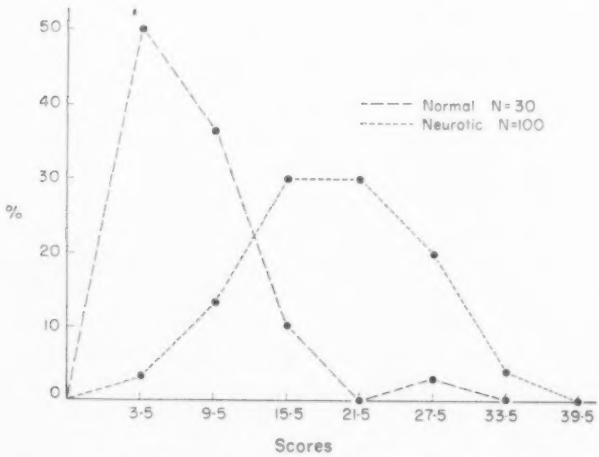

FIG. 2.—Frequency distribution of the neuroticism scores in the normal and neurotic groups.

DISCUSSION

Our investigations do not support the hypothesis that there is a negative correlation between allergological and psychological factors in asthma patients. Although these results cannot be considered as proof that such a negative correlation is nonexistent, they stress the need for convincing objective evidence supporting the view that asthma patients can be classified in an "allergologic" versus a "psychogenic" group.

But from our figures a more positive conclusion can also be drawn. This becomes obvious if the neuroticism scores of our asthma patients are compared with the scores

TABLE 2.—NEUROTICISM SCORES

	Mean	S.D.
79 female asthma patients	18·5	6·8
100 female psychoneurotic patients	19·1	6·6
30 normal females	7·3	5·3

of a group of 100 psychoneurotic female patients and with the scores of a group of 30 normal females (Table 2). The definitions of "normal" and "psychoneurotic" have been given above. There is a statistical difference between the normal individuals and the asthma patients ($P < 0{\cdot}01$) and also between the normal individuals and the psychoneurotic patients ($P < 0{\cdot}01$), but there is no statistically significant difference between our asthma patients and the psychoneurotics. SAINSBURY (1959) who also used HERON's method recently came to the same conclusion that asthma patients react to this test in the same way as psychoneurotics. These findings can be considered to support the hypothesis that asthma patients are neurotic. We wish to stress that no more than support is given and that no more can indeed be expected from our experimental set-up. Our patients were all females of a certain age group and they were a selected group at least by the fact that they had sought specialist treatment.

We found, however, no difference in neuroticism between a group of patients who were invited or came to visit a psychosomatic department and a group visiting a department for pulmonary diseases where anti-allergic treatment is stressed. This partially confirms the test-findings of LEIGH and MARLEY (1956) in a group of female asthma patients who came to an allergist when compared with a group seen by a psychiatrist. As regards the neuroticism in our asthma patients it is of course impossible to state from these experiments if this abnormal test behaviour has something to do with the etiology of asthma or whether it is a consequence of this chronic disease.

SUMMARY

(1) Several attempts have been made in the literature to group asthma patients according to the predominant etiological factor. A classification of asthma patients into an "allergic" and a "psychic" group can only be justified if a negative correlation between allergological and psychological factors can be demonstrated.

(2) Seeking support for this classification 79 adult female asthma patients were divided into two groups. Those patients in whom attacks of asthma could be provoked by the inhalation of nebulized allergens, were considered to be "allergic" (34 patients). The "non-allergic" group was composed of patients who either showed no positive skin reactions or in whom all positive skin reactions were followed by a negative

inhalation test (45 patients). In all patients the neuroticism was quantitatively and objectively determined by an independent observer by means of the "Two Part Personality Inventory", described by HERON (1955).

(3) No significant difference was found between the neuroticism scores of the "allergic" and the "non-allergic" groups.

(4) It was concluded that there is no convincing evidence available to support the classification of asthma patients into an "allergic" and a "psychic" group.

(5) There was no significant difference between the neuroticism scores of these asthma patients (18·5 ± 6·8) and those of a group of 100 female psychoneurotic patients (19·1 ± 6·6).

(6) The asthma patients had a considerably higher neuroticism score than a control group of 30 normal female subjects of the same age group (7·3 ± 5·3).

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URINARY CATECHOL AMINE LEVELS, GASTRIC SECRETION AND SPECIFIC PSYCHOLOGICAL FACTORS IN ULCER AND NON-ULCER PATIENTS*

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INTRODUCTION

A CONSIDERABLE body of information has been gathered which has suggested that the pathophysiology of duodenal ulcers is influenced by psychological factors operating through the effects of the central and autonomic nervous system on gastric physiology. However, until recent years, there has been a paucity of experimental studies in which multiple interacting predisposing and precipitating elements could be demonstrated. Many of the earlier studies were limited to the investigation of the specific physiological precipitants of duodenal ulcerations or the specific psychodynamic or personality correlates found in patients with peptic ulcers. (IVY *et al.* 1950; GROSSMAN 1951; HUNT and KAY 1954; ALEXANDER *et al.* 1934; KAPP *et al.* 1947; SZASZ *et al.* 1947; RUESCH 1948; GILDEA 1949; STREITFELD 1954; MINSKI and DESAI 1955, WEISMAN 1956).

The highlighting of a limited number of specific factors in each individual study led to the amassing of a large body of research data which has remained relatively unintegrated from an experimental point of view. Hence, there has been scant data to support the empirically developed concepts that peptic ulcer was a "psychosomatic" dysfunction. Because of this there has been no general agreement among the clinical specialties concerning the "proper" management program of patients with ulcers which would incorporate principles based on a consideration of the multiple determinants of the cause and the course of the disease.

The work which will be reported in this paper represents the convergence of three investigations which originally were unrelated. However, the data from the studies suggested an experimental design which would allow for the testing of an hypothesis of the interaction of psychological, gastric, physiological and neuro-humoral factors in the development of duodenal ulcers.

BACKGROUND STUDIES

The investigation which will be described in this publication was based on the findings of three separate studies.

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(A) The work of WEINER, THALER, REISER and MIRSKY (1957) and MIRSKY (1958) was concerned with a *propter hoc* psychologic evaluation of a group of healthy subjects together with the assessment of their serum pepsinogen levels. These subjects were a group preparing to enter an environmental situation which might have noxious or traumatic meaning to some of them (induction into the armed service.) The study was designed to evaluate the predictive value of biochemical, psychological and sociological factors which had been assumed to be related to gastrointestinal activity. In this study, the concentration of serum pepsinogen was used as an index of gastric secretion. "Hypo" and "hyper" secretors were studied in terms of their style of inter-personal interaction that could be inferred from psychoanalytically oriented interviews and derived from projective tests and other psychological techniques.

All of the subjects who had or who developed evidence of duodenal ulcer were found among the subjects with high pepsinogen values. Independent evaluation of the psychological data revealed that the subjects who developed peptic ulcer had displayed evidence of major unresolved and persistent conflicts with their need for dependent oral gratification. A psychodynamic constellation was formulated on the basis of several of the psychological tests (Blacky Test, Saslow Questionnaire, Rorschach, etc.) which correlated well with the hyper- and the hypo-pepsinogen secretor ratings, as well as, being able to predict the subjects who developed an ulcer (85 percent of the hypersecretor group were correctly selected on the basis of psychological criteria). The study indicated that neither a higher rate of gastric secretion nor specific psycho-dynamic constellation was independently responsible for ulcers. Together the two parameters constituted essential determinants in the precipitation of an ulcer on exposure to a social situation noxious to a specific individual.

(B) Recent studies by WADDELL (1956). as well as previous studies (BABKIN and SCHACTER 1950; DRAGSTEDT *et al.* 1950; GLASS and WOLF 1950;), have suggested that a high level of gastro intestinal secretory and motor activity may be a function of a parasympathetic-sympathetic imbalance, associated with excessive vagal discharge. Studies by WADDELL have also suggested that differences in urinary levels of catechol amines may be found in ulcer and non-ulcer patients and that these levels may reflect differences in sympathetico adrenal responsivity. WADDELL's studies have been particularly concerned with the influence of catechol amines and autonomic discharges on the gastric vasculature. These investigations have been concerned with the reduction in gastric secretion associated with vasoconstriction of gastric vessels and the increase in gastric secretion associated with vasodilatation.

In addition, other work by WADDELL (1956) has highlighted the role of the pyloric antrum in the acid secretory mechanism of the stomach. He has reported that the recovery of acid is reduced by antral exclusion and sleeve resection of the mid portion of the stomach. The magnitude of the effect on acid secretion is variable. But the reduction of vagal secretion in a response to all stimuli may be profound. Ulcer patients with antral resections secreted less acid under all conditions than ulcer patients with intact stomachs. But they responded to various stimuli and maintained a pH well within the range necessary to activate peptic digestion during all tests periods. (WADDELL 1956).

It is believed that the rate of gastric secretion is dependent in large part upon the tonic state of the vagal reflex centers which in turn are maintained by the continuous inflow of afferent impulses from many areas, particularly the mouth area and the antral area of the stomach. The principle effect of removal of the antrum in the experiments described by WADDELL is explained as a result of the withdrawal of an important source of afferent impulses which normally contribute heavily to the maintenance of a responsive state of reflex activity.

The relationship between the antrum and the reflex control of gastric secretory activity is conceived as analogous to that which exists between the carotid body and the reflex centres that control blood pressure. It is precisely this analogy which led the two research groups reporting in this paper to bring to bear their interests, experiences and techniques in an attempt to delineate some of the interrelationships between emotional, neurophysiological and gastric physiological factors.

(C) Studies of catechol amine and vascular correlates of specific emotional states. In one series of investigations the influence of emotional states on compensatory vascular reflexes (carotid sinus, aortic, etc.) activated by physical and drug stimuli producing a hypotensive effect in the head and neck region was studied (COHEN 1959). Adrenaline and noradrenaline levels were assessed as an index of response of the sympathetic nervous system and adrenal medulla. The experimental data suggested that catechol amine production was a determinant of or at least a correlate of an individual's vascular compensatory responses. In addition, the type and intensity of emotion present during the experimental situation appeared to alter the response to a massive physiologic stressor (human centrifuge)

or to produce a characteristic vascular response when a minimal vascular stimulus was introduced (Injection of small amount of parasympathetic mimetic drug). The effect of emotional arousal on vascular responsivity appeared to be mediated to a large extent by the differential release of adrenaline and noradrenaline. Hypotensive responses occurred in conjunction with low excretory levels of urinary noradrenaline and moderate or high excretion levels of urinary adrenaline. Subjects demonstrating this kind of vascular response pattern showed minimal aggressive behavior and a low level of angry, hostile, competitive feelings. At the same time, they appeared to be markedly anxious. Subjects with hypertensive responses show a minimal to moderate degree of anxiety with marked angry, hostile feelings and noticeable display of aggressive behavior. Their catechol amine excretion showed high levels of noradrenaline in the control and experimental specimens.

The association of specific emotional state and behavioral mode variations with catechol amine levels and vascular responses was speculatively thought to be due to the activation of specific hypothalamic areas and the selective release of neuro-hormones. It has been demonstrated by others that stimulation of specific hypothalamic areas causes the selective release of adrenaline and noradrenaline. (FOLKOW and EULEV 1954). Furthermore there is evidence that cells in the adrenal medulla may release adrenaline and noradrenaline independently and these cells may be innervated by different hypothalamic areas. (HILLARP 1953). The work of BARD (1949), CHAPMAN (1950), GELLHORN (1956) and HESS (1949) suggested other central mechanisms to account for the above relationships. For example, it has been demonstrated that electrical stimulation of the cerebral cortical, as well as, hypothalamic areas led to alterations in blood pressure. In addition it had been suggested that the anterior and posterior hypothalamus may exert a tonic effect on medullary vasomotor regulatory centers. Whether these areas are related to the hypothalamic areas which had been previously identified by direct stimulation studies as the areas exciting anxiety or rage responses remains a moot question. The evidence does suggest, however, that at least the adrenaline producing areas of the hypothalamus are anatomically similar to those portions which previously had been identified as centers for fear responses.

The above work suggested that there may be central mechanisms mediating specific emotional responses and that these mechanisms may be related to neural circuits concerned with the release of catechol amines, as well as, the activation of portions of the autonomic nervous system.

Urinary catechol amine levels were of interest then as possible correlates of specific behavioral modes and emotional states, as well as, being correlates of gastric activity and duodenal ulcer formation.

EXPERIMENTAL METHODOLOGY

(*A*) *Hypothesis and Approach*

The study which will be reported in this paper represents the combined effort of two research teams from two different universities utilizing techniques permitting the independent evaluation of specific psychological factors, gastric secretion and catechol amine urinary levels in ulcer patients and control subjects. The experimental physiological test situation was felt to have psychological implications which would highlight any psycho-dynamic differences between the two groups. The psychodynamic factors were those that had previously been described in ulcer patients in other studies.

It was hypothesized that a consistent relationship would exist between catechol amine levels and the presence or absence of duodenal ulcer as had been suggested by previous work by WADDELL and ZUIDEMA (1960). The previously identified relationship between specific psychological characteristics and catechol amine excretory rates was also anticipated in the subject population (COHEN, SILVERMAN *et al.* 1957, 1959). However, the psychological characteristics usually associated with various catechol amine levels were not expected in ulcer patients but would only be noted in those who showed characteristic catechol amine levels, as well as, an ulcer. The use of the psychologic criteria from the study of WEINER *et. al.* (1957) was an attempt to substantiate the findings of that study, as well as to suggest any relationships which might exist

VOL.
5
1960/6

between the psychologic correlates of catechol amine excretion and the psychological correlates of peptic ulcers.

(B) Experimental Design and Subjects.

Urine and gastric juice collections were carried out before and after administration of peptone broth, histamine and insulin in 10 white, male ulcer patients and 10 white, male, non-ulcer control patients who were chosen by the group at the Massachusetts General Hospital without any communication with the research team at Duke. The 10 ulcer patients had radiologically demonstrated active duodenal ulcers. The control patients had no evidence of duodenal ulcer. Seven of the control subjects were normal, healthy volunteer subjects and the remaining 3 were hospitalized for illnesses other than duodenal ulcer. (They had carcinoma of the rectum, chronic cholecystitis and a cholangeitis secondary to partial stricture of the bile ducts.) The ulcer and non-ulcer populations were made up of hospitalized and ambulant individuals who were matched as far as possible for age and socio-economic status. The choice of 3 control subjects with gastro-intestinal disease was made in an effort to determine whether any psychological responses, noted on the tests and felt to be specific for duodenal ulcers, might be associated with gastrointestinal diseases other than duodenal ulcer.

Each subject was tested on 2 separate days, The test began each day at 7.30 a.m. after an overnight fast. On the first day, the subject waited and then lay quietly in bed with his head inclined at a 45 degree angle. Most of this first hour was occupied with psychological testing. After one hr, the subject stood beside the bed to void the first urine sample. Immediately after this, a Levine tube was passed to the stomach and adjusted to aspirate freely. Twenty min later, the collection of gastric juice was begun. Six 10-min "basal" samples of gastric juice were collected. At the end of this period, the patient again stood to void a second sample of urine. Both urine collections were referred to as "basal" samples. After the second voiding, 80 c.c. of peptone broth were introduced into the tube which was then clamped for 20 min. The stomach was then emptied and six more 10-min samples of gastric juice were obtained. At the end of this period, the bladder was again emptied. Histamine diphosphate 0.5 mg was then administered subcutaneously and six more 10-min samples of gastric juice were collected. At the end of the hour, a final collection of urine was made.

On the second day of testing, a similar routine was followed. After the first 2 hr (during two "basal" urine samples and one "basal" gastric collections were obtained) 12 units of regular insulin were injected intravenously. Thereafter, 30-min samples of gastric juice were collected and the patient voided $1\frac{1}{2}$ hr and 3 hr after insulin administration. Blood sugar concentrations were measured before the insulin was given and 30 and 60 min thereafter. (It might be noted at this point that blood sugar concentrations were reduced to below 50 mg per c.c. in all ulcer patients and in all but one control patient.)

After the final collection of the urine specimen on each day's testing, the subject was interviewed by a member of the surgical team using a list of nine questions which had been prepared by the group at Duke for this particular experiment. The interviewing was carried out by a member of the surgical team who had had previous experience with the use of interviews as an experimental tool.

The specific instructions for the administration of various psychologic tests (which

will be described in subsequent sections) had been forwarded to the surgical group. The psychologic tests and interviews were recorded and the transcripts were forwarded to the group at Duke who evaluated them without any information regarding the patient's name or diagnosis, or any of the gastric secretory or catechol amine data. The transcripts were reviewed prior to their being forwarded to the group at Duke so that all possible cues which would suggest the presence of an ulcer or which would suggest whether the subject was a volunteer, healthy subject were removed from the protocols.

(C) *Measures*

(1) *Catechol amine excretion.*

Immediately after the urine collections, the volume of each urine sample was measured and the entire specimen acidified to a pH of 2·3 with 6 N hydrochloric acid. The samples were frozen and stored for later analysis. The determination of adrenaline and noradrenaline in these samples was made by DUTOIT'S (1959) modification of the fluorometric method of FLODDING and VON EULER (1956) utilizing a cation exchange resin method of purification.*

(2) *Gastric secretions.*

The gastric specimens were examined† for the volume in cc's per hour, pH of the specimen, free acid in mEquiv. per l., free acid in mEquiv per hr, chloride mEquiv per l. and chloride mEquiv per hr.

(3) *Psychological measures.*

The first morning that the subject was tested, he was given a set of general instructions prior to the time that he was intubated. Following the instructions, he was then given the following tests:

(a) Focused Thematic Test
(b) Draw a Person Test
(c) Cards 2 and 3 from the Blacky Test
(d) Saslow Questionnaire
(e) Focused Interview

(a) *Focused Thematic Test* (SILVERMAN *et al* 1957). The subjects were presented 4 cards from this test in sequence and were asked to make up a story for each picture. The story did not have to be of any specific type. After the subject had given a story, he was then asked to mention what events might have led up to the story in the picture and what was the possible conclusion.

The stories that the subjects told in response to each card were scored on a 0 to 3+ basis in the following areas (according to criteria described in previous publications).

(1) A behavioral mode of the hero (with an active, aggressive, mastering, impulsive description being scored 3+ and a passive, yielding submitting hero scored 0).

Behavioral mode score. This score is obtained on the basis of a 0 to 3+ scoring in the following areas:

(a) The activity portrayed in the story as related to the cues which are actually presented in the picture.

(b) Degree of independence or dependence demonstrated in the behavior of the hero while carrying out the activity of the story.

(c) The level and type of aggressivity displayed in the behavior or thinking of the hero, considering the type of expressive mode, the directness of expression, the remoteness of expression.

(d) The degree of discomfort with aggressive behavior feelings and ideas which are expressed.

(e) The degree of mastery that the hero demonstrates.

* The fluorometric method was a modification of the VON EULER and FLODDING ferricyanide modification of the Lund method. Instead of using the VON EULER and FLODDING preferential oxidation technique, a multiple filter system was worked out for the simultaneous estimation of adrenaline and noradrenaline.

† After the measurement of the volume of each sample of gastric juice, the pH was determined on a Beckman calomel glass electrode pH meter. The acidity was titrated to a pH of 3·5 with 0·1 N in sodium hydroxide by an electrometric method and the chloride concentration was measured by the method of WILSON and BALL (1928).

VOL.
5
1960/6

(f) Impulsivity. The more the hero of the story acts on a wish feeling, or impulse without restraint and without consequence, the higher is the score.

The stories are graded on the basis of a scoring key. A final "behavioral mode" score is tabulated by averaging the sum of all the above factors in all the stories so that a score is obtained for the behavioral mode on a 0–3 continuum. This score is considered a reflection of the behavioral mode of the subject on an aggressive-passive scale.

(2) The emotional state (a clearly stated affect of anger or happiness is scored 3+ and a clearly stated affect of anxiety or depression is scored 0).

Emotional state score. The emotional state of the hero is also scored. The type of affect and the manner in which it is expressed are the major criteria used to obtain a score in this area. If the affect is stated, the score is 3+; strongly implied, 2+; inferred, 1+; and absent, 0. Each of four affects are scored separately: anger, anxiety, depression, happy, satisfied content.

The emotional state referred to the level of anxiety, anger and depression noted in the test protocols. The behavioral mode was related to the direction, type, and intensity of aggressive expression. It was these parameters which had been related in previous studies to the level of catechol amine. (COHEN and SILVERMAN 1959; SILVERMAN *et al.* 1957).

Subjects with highest aggressive behavioral mode scores, highest anger affect ratings, lowest anxious and depressed affect ratings were predicted to have the highest noradrenaline and lowest adrenaline excretions during the period of time that the tests were administered. (Basal Period No 1 on Day 1).

The scores were further predicted to discriminate ulcer and non-ulcer patients if the catechol amine levels discriminated these patients.

(b)(c)(d) Psychological test battery for "Hyper" and "Hypo" secretor factors D.A.P., Blacky Test and Saslow Questionnaire. The D.A.P., Blacky Test and Saslow Questionnaire were used in this experiment because specific aspects of these tests had successfully discriminated in a previous study (WEINER *et al.* 1957) (12) the subjects who had high pepsinogen levels and developed peptic ulcer from those with low pepsinogen levels who did not develop ulcers.

(b) *Draw a Person Test.* The drawings were evaluated by an "independent" rater who was given a series of categories to grade from the drawings. The rater was not told how the scores would be correlated or with what measures it would be compared. The rater's evaluation was then scored for the presence or absence of the following factors*.

Hypersecretor Factors

Immature, boyish, asexual drawings
Male figure reflecting dependent, compliant, and oral needs
A dominant, controlling, or aggressive female figure
Diffuse anxiety and/or depressive features

Hyposecretor Factors

Paranoid features
Pseudo-masculine features
Conflicts in the area of passivity and activity

The raters evaluation were scored as follows:

2+—"hyper" secretor factor present or "hypo" secretor factors absent.
1+—if it was equivocal
0 —"hyper" secretor factor absent or "hypo" secretor factor present.

Patients with peptic ulcer were predicted to have a higher "hyper" secretor score than control subjects. A mean score over 1+ was categorized as "hyper" secretor and lower than 1+ as "hypo" secretor.

(c) "*Blacky*" *Test.* The subject was given the same instructions as on the F.T.T. Cards 2 and 3B were used since they most accurately discriminated the high and low pepsinogen secretor subjects in the study of WIENER *et al.* (Expression of anger on Card 2 and denial of aggression on card 3B).

* Dr. B. M. SHMAVONIAN, Chief Psychologist of the Division of Psychophysiologic Research of the Department of Psychiatry, Duke University Medical Center, rated the test protocols. He had not been a participant in this project and had no information other than a list of categories on which he was asked to score the drawings.

The test was scored in a manner similar to that described in WEINER *et al.* paper. However, there were slight modifications based on the scoring techniques used by the investigators in evaluating angry affect and aggressive behavioral mode for projective test stories.

Subjects directly expressing anger and describing aggressive behavior consistent with the degree of anger expressed were predicted to be the least likely to have an ulcer (or low in hypersecretor factors.) i.e. they were scored 0 for hypersecretor.

Discomfort with anger and/or agression was interpreted on the basis of the absence of both from the stories or an inconsistency between the angry affect and aggressive behavior described. The subjects with the highest level of discomfort were predicted to be most likely to have an ulcer (on 2+ "hyper" secretor score)

(d) *Saslow Questionnaire* (32). This questionnaire required the subject to indicate by a "yes", "usually", "often", "rarely", "never", reply his ability to express and handle angry and anxious feelings.*

The subject was asked to encircle one of the above responses which most closely matched their feelings.

There was a series of questions related to anger and a series related to anxiety which required the subject to state whether they express these feelings immediately, whether they suppress feelings, whether they express as much as they feel, whether they express the feeling to the person who created the feeling? They are then asked if they hold in their feelings, do they feel ill? If they answer "yes" to this question, they are then asked to circle any symptoms which are listed (GILDEA 1949) which develop when they hold in their feelings.

Immediate, direct and complete expression of either feeling was scored 0 for hypersecretor factors. The suppression of feelings with an indication that somatic symptoms developed when emotionally aroused and the indication of four or more symptoms in the list presented on the questionnaire were scored as hypersecretor factors and where predicted to be found in patients with ulcers. Hence, the subjects who described the most difficulty with the outward expression of emotions (anger and anxiety) and the largest number of somatic symptoms when emotionally aroused were predicted to be most likely to have an ulcer.

(e) *Focused Interview.* Following the gastric secretory and urine collections on each of the two days, the subjects were interviewed by one member of the surgical team. The interview was recorded and the transcript was typed, it was carefully reviewed in order that all cues be removed which might suggest whether the subject had an ulcer or whether the subject was a volunteer. The interview was structured and consisted of a series of nine questions which has been prepared by the research team at Duke.

The questions were focused on the subject's perception of the test situation, the examiners, and the individual test stimuli. The behavior and feelings which the subject experienced were explored. An attempt in general was made to evaluate two major areas:

(1) The emotions which the subject experienced as indicated by the verbalizations of the subject during the interview, as well as, the associations of the subject. The purposes of the question was to highlight the emotions experienced in relation to the test situation and the test stimuli. The impulses and feelings which were aroused were evaluated with a particular attempt made to determine the kind of psychologic adaptational or defensive mechanisms which the subject utilized to master the experimental situation.

(2) The fact that a tube was placed in the gastrointestinal tract after the subject had been required to fast for twelve hours and the fact that the subjects were dependent on medical authority figure, either in relation to the test or the treatment situation, were considered "orally" significant stimuli. Because of this, it was felt that the psychodynamic behavioral and thought patterns usually noted in patients with a peptic ulcer should be exaggerated when their thoughts, feelings, expectations, and reactions to the experimental situation were explored.

The responses of the subjects to the interview questions were compared and evaluated on the basis of some of the psychologic factors described as discriminating the ulcer and non-ulcer (as well as hyper and hyposecretor) groups in the study by WEINER *et al.* (1957). Predictions were made as to whether the subject was an ulcer patient or a non-ulcer patient on the basis of the amount of "hypersecretor" psychologic type factors which were noted in the interviews.

* The questionnaire used in this study was a slight modification of the original questionnaire. The criteria of prediction were based on the study reported by WEINER *et al.* and not those from the original study of SASLOW.

VOL.
5
1960/6

The questions were:

What did you think of the test?

How did you feel during the test?

What did you think the test was for?

How do you think it could be made easier?

What did you think about the tube? Needle? And what kind of reaction did you have from the tube? Needle? Injection?

What did you think is the most important reason for giving this test?

What would be the most important thing that could result from this test?

Have you ever been exposed to a situation similar to this? How did you feel? Did you ever experience feelings like you did during this test regardless of whether it was a similar situation or not?

Have you found out this test did not show anything important or would not be helpful to you, how would you feel?

The criteria of predictions for the interview were:

(1) Perception of test situation, examiners and test procedures. It was predicted that patients with peptic ulcers would perceive the test situation as

(a) a source of help, i.e. as a situation which would bring them personal benefit either as a treatment or leading to a treatment which would help him: or that the test would help by leading to a diagnosis of his condition (with the implication that he would then be helped.)

It was thought that the ulcer patient would express a need for external help which his dependency on the test would reflect. There would be no indication of a wish to master the test situation and there would be a denial of any bodily discomfort produced by the test.

(b) the non-ulcer patient would be more prone to perceive the testing situation as a competitive one in which there would be attempts by the patient to demonstrate their ability to master it. Furthermore, this might be shown by attempts to deny that the test was hard or that they were hurt in any way.

They would perceive the test more impersonally and not expect any direct benefits. The non-ulcer patient would not feel the test was beneficial personally although he might state it had some value as a therapeutic, diagnostic or research tool.

(c) The ulcer patient would further perceive the test situation in terms of their preoccupations with the tube (e.g. as a source satsifying or leading to satisfaction of their needs to be fed, taken care of). In contrast to this, the non-ulcer patient might show more concerns with the psychologic test portion of the experiment, concerns about having their personality investigated, having things about them revealed and demonstrate a high degree of suspiciousness. This prediction was based on the more frequent occurrence of paranoid trends (e.g. suspiciousness) in the hyposecretor group in previous investigations (WEINER *et al.* 1957).

(2) The ulcer subjects would show a greater tendency to accept the authority of doctors and hospital personnel without question and without complaint. The ulcer subject would demonstrate a greater tendency to submit and passively yield to the wishes of external objects, particularly authorities. The ulcer subject would show a greater tendency to comply with the wishes of the authorities and submit to unpleasant procedures without complaint. He would also show a greater tendency to please and placate authorities.

(3) The subjects who demonstrated an emotional state of high anxiety, particularly if it occurred in relationship to areas which appear most relevant to oral dependency conflicts, then the more likely the subject was to have peptic ulcer. This was even more likely if they also showed an inhibition or denial of aggressive impulses and angry thoughts about the test situation. There would be greater tendency in the ulcer patient to deny any expression of affect. There would be more evidence noted in the ulcer patient of many maneuvers to obtain or retain the external support and not express their angry feelings. Hostility which was aroused would produce anxiety and guilt and would be handled by a denial, internalization, rationalization and displacement.

The subjects without peptic ulcers would be most likely to react to sources of discomfort with hostility which they are able to express more easily than the ulcer patients. The non-ulcer subjects would also demonstrate fewer problems in regard to dependency and less dependency on the external authorities.

(4) It was predicted that the non-ulcer patient or the hyposecretor would show a greater amount of pseudo-masculine trends with attempts to demonstrate masculine over-compensation or defenses

against hostile feminine identification. This would be associated with more problems referable to masculinity and feminity, activity in passivity as well as conflicts over sexual identification.

(5) The non-ulcer patient would display more conflicts, wishes or needs in relation to narcissism. Associated with this, they would exhibit more problems relative to internal bodily discomfort.

RESULTS

Differences between Ulcer Patients and Control Subjects

(A) *Psychological Test Battery for "Ulcer" Psychodynamic Characteristics*

(1) *Draw-A-Person Test.* Nine patients and 10 controls completed the D.A.P. Test. Table 1 shows the results of the evaluations of the criteria mentioned with previous section.

TABLE 1.—"HYPER" AND "HYPO" SECRETOR SCORES AND PREDICTION OF ULCER

	Predicted to have ulcer ("hyper")	Not predicted to have ulcer ("hypo")
Subjects with ulcer ($N = 9$)	7	2
Control subjects ($N = 10$)	2	8

TABLE 2.—PREDICTION OF ULCER "HYPER" AND "HYPO" SECRETOR SCORES ON SASLOW

	Hypersecretor	Hyposecretor
Ulcer ($N = 9$)	6	4
Control ($N = 10$)	3	6

A Chi Square test of the significance of difference of ulcer and control subjects for "hyper" secretor scores vs. "hypo" secretor was significant at 0·05 level ($P = 0{\cdot}05$).

(2) *Saslow Questionnaire.* Nine ulcer subjects and 10 control subjects completed this questionnaire. Table 2 shows the distribution of the subjects' scores on this questionnaire in regard to their being in the hyper or hyposecretor range on the basis of the criteria described previously.

A Chi Square test of difference of ulcer and non-ulcer group for hypersecretor scores and hyposecretor scores was not significant.

(3) *Blacky Test.* The scores of 10 ulcer and 10 control subjects are listed on Table 3.

Difference of ulcer and control subjects the number of "hyper" secretor scores vs. "hypo" secretor was significant at $P = 0{\cdot}01$.

(4) *Overall Rating* on combined "hyper" and "hypo" secretor scores of D.A.P. Blacky and Saslow. The average of the actual scores of the 10 ulcer and 10 control subjects on all three tests for "hyper" and "hypo" secretor factors is shown on Table 4.

VOL. 5 1960/6

When the score for all 3 tests was determined, the difference in the control and ulcer group was significant with $P = 0{\cdot}05$.

(B) *Post-Test Interview Ratings*

The replies of 10 ulcer and 10 control subjects to the nine questions asked in the post-experimental interview were scored on the basis of "hyper" and "hypo" secretor psychological factors derived from the study reported by WEINER *et al.* (1957) and modified by the investigators for the specific experimental situation.

TABLE 3.—"HYPER" AND "HYPO" SECRETOR SCORES ON BLACKY

	Predict ulcer	Not predict ulcer
Ulcer	8	2
Control	1	9

TABLE 4.—"HYPER" AND "HYPO" SECRETOR SCORES ON D.A.P., BLACKY AND SASLOW

	Hyper-secretor score	Hypo-secretor score
Ulcer ($N = 10$)	9	1
Control ($N = 10$)	3	7

Each expression or statement evaluated as a "hyper" secretor factor was scored (+) and each statement evaluated as a "hypo" secretor factor was scored (−).

The final score for each factor was obtained by adding the number of times it had been identified in the subjects' responses to the nine questions. Table 5 lists the sum of the ulcer patients and control subjects' score in each of the eight areas which were evaluated in the nine questions. The total scores of each individual subject is also shown on Table 5. The total score for each individual was obtained by adding the total hypersecretor factor scores (+) and subtracting the sum of the hyposecretor factor scores (−). Subjects with a final score in (+) range (hypersecretors) were predicted to be most likely to have an ulcer and subjects with a score in (−) range were predicted to be least likely to have an ulcer.

The subjects' interview responses were scored separately on each day. The data presented in this paper which is charted on Table 5 is a summary of the *overall* score of the first and second day interviews. Later publications will compare the psychological, physiological and endocrinological responses of the first and second test day.

The table shows that 9 of the ulcer patients had hypersecretor scores (+) and 9 of the control patients had hyposecretor scores (−). The difference between the groups was significant (using a Chi Square test, $P < 0{\cdot}001$).

The subjects have been listed so that they are rank ordered from highest "hyper" secretor score (+) to lowest "hypo" secretor score (−). The result is rather striking in that except for one tie (an ulcer and control subject with rank order of 10·5 and scores of −1 there is a perfect division of ulcer and control subjects.

TABLE 5.—SCORING OF POST-EXPERIMENTAL INTERVIEW IN ULCER PATIENTS AND CONTROL SUBJECTS

	"Hyper" secretor factors (scores +) Combined score of all subjects				"Hypo" secretor factors (scores −) Combined score of all subjects					Final scores of ulcer patients and control subjects
	Perceive test situation as source of personal help (dependency needs)	Evidence of inhibition of angry feelings and aggressive impulses	Evidence of self-depreciation, self blame, guilt	Evidence need to comply, submit, placate authority	Perceive test impersonally unrelated to own needs, not source of benefit. Concerned with competition and mastery	Direct expression of angry feelings and aggressive impulses	Evidence of suspiciousness and "paranoid" type thought trends	Concerns with masculine adequacy, and narcissistic needs	Final score (hyperhypo)	Ulcer patients / Control subjects
Ulcer patients ($N = 10$)	+44	+30	+5	+28	− 6	−14	− 3	− 2	+82	+21 / − 1 +13 / − 3 +12 / − 5 +11 / − 6 +10 / − 6 + 6 / − 7 + 5 / −10 + 3 / −11 + 2 / −17 − 1 / −18
Control subjects ($N = 10$)	+14	+6	+2	+5	−28	−51	−20	−11	−83	Difference of ulcer and control using Chi Square test significant at $P < 0{\cdot}001$

VOL. 5 1960/61

For a "factor" to be scored in the subject's answer, clear and direct evidence has to be noted. If a statement or expression implied or inferred some feeling or percept, it was not scored.

Some illustrations of the type of expression which were scored and expressions which were not scored are illustrated in the following section.

Question 1: *What did you think of the test*?

Control subject. "The tube was a bit uncomfortable, the rest went all right."
(1) Expression of discomfort—"Hyposecretor" factor (−)
Ulcer patient: "I think the doctors are trying to do right. My getting into such a condition that's why I'm the patient."
(1) Self-depreciation (+)
(2) Placate doctors (+)
(1) and (2). "hypersecretor" factors 2(+)
(3) Implied need for dependency and help from doctors—not scored.

Question 2: How did you feel during the test?

Control subject: "It was a little inconvenient having that tube down there. I felt like I wanted to swallow and couldn't, but I didn't feel any pain."
(1) Expresses discomfort with test
(2) Concern in area of mastering situation and being an adequate male (i.e. wish to be able to act, not be overwhelmed or feel pain)
(1) and (2) "hyposecretor" factors 2(—)
Ulcer patient: "I felt it was worthwhile and for my benefit."
(1) Perceives test as being source of help for him. 1(+)

Question 3: What did you think the test was for?

Control Subject: "I know it must be some kind of research. I wouldn't imagine what the tube had to do with the pictures. I couldn't connect the two, it had me baffled."
(1) Perceives test in impersonal manner of no direct benefit to him. 1(−)
(2) Concerned about inability to understand and master situation 1(−). Scored for two hyposecretor factors 2(−)
Ulcer Patient: "To find out what's wrong with me."
(1) Perceives test as being source of personal help. Scored for hypersecretor factor. 1(+)

Question 4: "Could you think of any way test could be made easier?"

Control Subject: "Probably make it shorter."
(1) Expresses criticism. Score for hyposecretor factor. 1(−)
Ulcer patient: "In my estimation couldn't make it better."
(1) Need to placate. Scored for hypersecretor factor. 1(+)

Question 6: "What do you think was the most important reason for giving this test?"

Control Subject: "To explore my case so that I might be used for future records." (This control subject was hospitalized with Carcinoma of the rectum).
(1) Test not seen as source of personal help (−)
(2) Suggestion of feeling of being exploited. Implied but not scored as hyposecretor factor.
Ulcer Patient: "To see my functioning and my trouble and to see best way to cure it."
(1) Test seen as source of personal help. Scored for hypersecretor factor. (+)

Question 7: "What would be the most important thing that could result from this test?"

Control Subject: "To make it easier for doctors to diagnose ulcers. You might have learned something."
(1) Perceives test as being useful to doctors, not himself. Score for hyposecretor factor. (−)
Ulcer Patient: "To help me be myself."
(1) Test perceived as source of help for patient. Score for hypersecretor factor. (+)

(C) *Focused Thematic Test*

The scores on this test were expected to relate to the ratio of catechol amines in the subjects' urine. In previous studies, the subjects whose test responses had been scored as demonstrating a high level of aggressive impulses and angry affect had been found

TABLE 6.—RELATIONSHIPS OF SCORES ON FOCUSED THEMATIC TEST (FTT)

(A) Correlation of F.T.T. score, catechol amines and gastric secretion

		Rank order of	Correlation and significance
Rank order of scores on F. T. T. (High rank order for score reflecting aggressive behavioral mode, anger and low anxiety	Correlated with:	Total catechol amine level and adrenaline % during psychological test period (Basal Day 1)	$r_s = +0{\cdot}57$ $< 0{\cdot}02$ $> 0{\cdot}01$
		Total catechol amine level and adrenaline % (a) "Basal" specimen day 1 & 2 combined— (b) After insulin— (c) All specimens—	P = N.S.
		Gastric secretion (volume and free acid) (a) During basal day 1 psychological tests— (b) "Basal" day 2— (c) Basal day 1 & 2— (d) After stimulation— (e) All specimens—	P = N.S.

(B) Prediction of ulcer from F.T.T. score

	Predict ulcer (Low aggression and anger; high anxiety score)	Not predict ulcer (High aggression and anger; low anxiety score)
Ulcer patients ($N = 9$)	4	5
Control subjects ($N = 10$)	2	8

P = N.S.

to have high level of nor-adrenaline excretion and low level of adrenaline excretion in urinary specimens. Subjects who presented stories which were scored as showing a high level of anxiety, a low level of anger and aggressive impulses had low urinary level of nor-adrenaline and high level of adrenaline. Hence the correlation which was expected in this study was between the FTT score and the catechol amine levels.

It was expected that if the catechol amine levels showed significant differences in ulcer and control subjects, then a correlation might be found between FTT score and the presence or absence of ulcer.

VOL. 5 1960/6

The correlation of the scores on the FTT and the catechol amine urinary excretion is seen on Table 6. The catechol amine levels charted for Day 1, Basal Period 1, are those which were obtained from the urine specimens collected *during the time* the psychological tests were being taken.

The subjects' FTT scores were rank ordered on the bases of their behavioral mode and emotional state score. The subjects' catechol amine levels were rank ordered on the bases of the total catechol amine level and the percentage of adrenaline because in previous studies, the FTT correlated with the ratio as well as the level of adrenaline and noradrenaline. Hence, a high catechol amine level and a low adrenaline percentage had the highest rank order.

TABLE 7.—PREDICTION OF ULCER FROM ALL PSYCHOLOGICAL MEASURES

	Draw a person test	Saslow questionnaire	"Blacky" test	Focused interview	F.T.T.	Prediction based on average rating on all measures
Ulcer patients	7/9 predicted to have ulcer	6/9 predicted to have ulcer	8/10 predicted to have ulcer	9/10 predicted to have ulcer	4/9 predicted to have ulcer	9/10 predicted to have ulcer
Control subjects	8/10 not predicted to have ulcer	6/10 not predicted to have ulcer	9/10 not predicted to have ulcer	10/10 not predicted to have ulcer	8/10 not predicted to have ulcer	9/10 not predicted to have ulcer
Significance using Chi Square	$P = 0{\cdot}05$	P = N.S.	$P = 0{\cdot}01$	$P = 0{\cdot}001$	P = N.S.	$P < 0{\cdot}01$

The correlation coefficient between FTT score and catechol amines was 0·57 which was significant at better than the 0·02 level, but less than 0·01 level.

Table 6 also shows the relationship of FTT scores to the catechol amine levels and adrenaline per cent found.

(a) in the urine specimen of "Basal" day 1 and Day 2 combined.

(b) in the urine specimen after insulin injection. (The insulin injection was assumed to be a stimulant to the hypothalamus.)

(c) in the average of all urine specimens.

The correlation described previously was between the FTT score and the catechol amine level in the urines collected during the time the FTT was being taken. From the results which are shown, it can be seen that the FTT score correlated only with the catechol amine levels during the time the tests were being administered.

The relationship of FTT scores with the presence or absence of ulcers is indicated at the bottom of Table 6. The subjects who had high aggressive behavioral mode and high anger and low anxiety scores were predicted to be least likely to have ulcer (if high noradrenaline levels were found in the control subjects and low noradrenaline levels found in ulcer patients.) The FTT did not discriminate ulcer and non-ulcer subjects.

The scores on the FTT were compared with the scores on the psychological test battery for "hyper" and "hypo" secretor factors (DAP, Saslow and Blacky. A rank order correlation was done and a negative correlation was found (r_s, − 0·36). The correlation just missed being significant at a 0·05 level (r_s, − 0·377 would have been significant at a 0·05 level.)

The scores on the FTT showed no correlation with the actual gastric secretion* of the subjects during the test period.

(D) *Predictions from All Psychological Measures*

Table 7 summarizes the differences between ulcer and control groups in the psychological areas tested. The table lists the predictions based on a score derived from a consideration of all psychological measures. The subjects' final scores on each test (++ score for hypersecretor, + equivocal and 0 for hyposecretor range) were averaged and a final score for all psychological measures was obtained.

* Gastric secretion refers to the total volume an the free acid (mEquiv/l.)

On the basis of this score, 9 out of 10 ulcer and 9 out of 10 control subjects were correctly predicted. The significance of difference using a chi square test was significant at better than a 0·01 level ($P < 0·01$).

None of the scores on the psychological tests individually (DAP, Saslow, Blacky, FTT) or the score of combined test battery correlated with the gastric volume and free acid secreted during the time the tests were administered.

TABLE 8.—GASTRIC SECRETION IN ULCER PATIENTS AND CONTROL SUBJECTS

Experimental period	Measure	Ulcer patients	Control subjects
"Basal" Day 1	*Volume	52 ± 6·5‡	55 ± 9·9
	†Free acid	15 ± 5	23 ± 6·9
After pepton broth	Volume	97 ± 17	79 ± 14·4
	Free acid	50 ± 7·5	40 ± 10·9
After histamine	Volume	134 ± 18·5	104 ± 17
	Free acid	77 ± 7	59 ± 12·2
"Basal" Day 2	Volume	68 ± 14·9	52 ± 12·2
	Free acid	30 ± 6·3	15 ± 4·4
After insulin	Volume	114 ± 17·2	79 ± 13·5
	Free acid	60 ± 6·9	44 ± 10·7

* Volume in ml/hr.
† Free acid in mEquiv/hr.
‡ (± = Standard error).
None of the Differences were significant at $P = 0·05$ level using the Chi Square test.

The rank order correlation of the scores of the subjects' pre-intubation psychological test battery for "hyper" and "hypo" secretor psychological factors and the "hyper" and "hypo" secretor scores on the post intubation interviews was significant. ($r_s = +0·63$, $t = 3·44$ and $P < 0·001$).

(E) *Gastric Secretion in Ulcer Patients and Control Subjects*

The gastric secretory data will only be summarized in this paper. A more complete presentation of the data and a more thorough discussion of the data can be found in other publications. WADDELL *et al.* (In press).

Table 8 summarizes the mean values (and standard errors) of some of the gastric secretory data of the 10 ulcer patients and 10 control subjects. The values were obtained during the "Basal" periods of Day 1 and 2, after a peptone broth, histamine and insulin stimulation.

Values for the total volume (cc/hr) and free acid (mEquiv/l.) are shown. Free acid (mEquiv/hr) and chlorides (mEquiv/l. and mEquiv/hr) were also determined, but are not shown on this chart.*

The mean total volume and mean titratable acidity of the gastric juice were higher and the mean pH was lower in almost all periods for the ulcer patients than for the control patients; however, the variation was marked, and only one of the differences between the ulcer and control group even reached even an 0·1 level of significance with a two-tailed test. (The "*P*" had to reach 0·05 level to be considered significant.) Hence, there were no striking differences in the gastric secretory values when the ulcer and control subjects as a group were compared, although rather marked individual differences were noted.

* These values did not indicate anything different than observations noted with free acid (mEquiv/l.) and volume. They have been omitted for the sake of brevity.

VOL. 5 1960/6

(F) *Catechol Amine Excretion*

Tables 9 and 10 summarize the results of catechol amine excretion during basal periods and after stimulation.

(1) Noradrenaline Levels. (Table 9). (a) "*Basal*" *Period.* The difference between the two groups with respect to excretory rate of noradrenaline reached the 0·02 level of significance with the control

TABLE 9.—NORADRENALINE URINARY EXCRETORY LEVELS IN ULCER PATIENTS AND CONTROL SUBJECT (μg/hr)

	"Basal"	After peptone	After histamine	After insulin (0–90 min)	After insulin (90–180 min)
Control subjects Mean S.E.	2·38 ±0·36	2·39 ±0·40	2·45 ±0·51	3·12 ±0·60	2·49 ±0·64
Ulcer patients Mean S.E.	1·31 ±0·20	0·85 ±0·31	2·40 ±0·83	1·48 ±0·23	0·88 ±0·24
t value	2·60	3·05	0·05	2·55	2·34
P	0·02	0·01	N.S.	0·05	0·05

TABLE 10.—ADRENALINE URINARY EXCRETORY LEVELS IN ULCER PATIENTS AND CONTROL SUBJECTS (μg/hr)

	"Basal"	After peptone	After histamine	After insulin (0–90 min)	After insulin (90–180 min)
Control subjects Mean S.E.	0·50 ±0·09	0·63 ±0·26	0·37 ±0·10	3·18 ±1·0	2·53 ±0·53
Ulcer patients Mean S.E.	0·32 ±0·06	0·33 ±0·08	0·68 ±0·41	2·36 ±0·38	1·22 ±0·28
t value	1·65	1·09	0·73	0·76	2·18
P	N.S.	N.S.	N.S.	N.S.	0·05

subjects excreting higher levels than the ulcer patients. (b) "*Stimulation*" *Periods.* During periods of stimulation with peptone broth and insulin, the mean noradrenaline output of the ulcer patients was lower than that of the control patients. The difference in noradrenaline levels for the control and ulcer patients after peptone administration was significant at 0·01 level. Ninety minutes after insulin administration, the differences were significant to the 0·05 level and 90–180 min after insulin, the differences were significant to a 0·05 level. In all instances, the differences were characterized by a higher level of noradrenaline in the control subjects than in the ulcer patients. Only after the

administration of histamine was there no significant difference noted and the mean levels of noradrenaline in the ulcer and control subjects were almost identical.

(2) *Adrenaline levels.* The mean adrenaline levels were higher in the control subjects than in the ulcer patients, but there was much less consistency and much greater overlap than in the case of noradrenaline. The difference in adrenaline level during the "Basal" periods was not significant. After peptone broth, there was no significant difference and this was also true after the histamine period. In fact, the adrenaline levels in ulcer patients were higher than the adrenaline levels in the control patients after the administration of histamine. (This was the only instance when this occurred.) 90 min after insulin there was no significant difference between adrenaline levels of ulcer and control groups. However, (180 min after insulin, the control group's level was higher than that of ulcer group. The difference was significant ($P = 0{\cdot}05$).

(3) *Response to insulin.* The ulcer patients had lower noradrenaline excretory rates than the control patients before the injection of insulin and during the first ninety minutes following the injection the difference between the two groups became more pronounced. However, the difference in mean response to stimulation by hypoglycemia between the ulcer and control groups did not attain statistical significance at the 0·05 level but was significant only at 0·1 level. Nevertheless, the trends suggested by the data were that a state of hypoglycemia produced by insulin injection led to a more marked change in noradrenaline level in the control group.

(4) *Response to histamine.* The responses of the two groups to Histamine was striking in that this was the only situation in which the level of noradrenaline in the ulcer group was not significantly lower than the level of noradrenaline in the control group.

The average response of the two groups was as follows:

Mean level before histamine injection	Mean level after histamine	Mean response
Noradrenaline		
Ulcer—0·9 μg/hr	2·4	+1·5 μg
Control—2·4	2·7	+0·3 μg
Adrenaline		
Ulcer—0·3 μg/hr	0·7	+0·4
Control—0·6	0·4	−0·2

The mean response difference did not attain any statistical significance due to the marked variation in the degree and direction of response within each group and the overlap between groups.

(5) *"Basal" specimen.* The comparison between "basal" catechol amine output of ulcer and control patients reported in previous section is not based on single samples, but on the combined figure of four separate specimens (pre and post intubation resting specimen on Day 1 and Day 2). This multiple sampling technique was used to minimize the influence of factors associated with changes in test environment, which might influence the catechol output.

When the four "basal" specimens were considered separately, the noradrenaline level in the ulcer patient was found to be lower than that of the control subject at a 0·05 level for three of the specimens and one at 0·1 level (not significant) using two-tailed test.

Three of the four comparisons indicated a lower adrenaline output in ulcer patients but none of these differences were statistically significant.

(6) *Urine volume.* The results strongly suggested that ulcer patients had lower mean noradrenaline urinary levels under basal conditions, after peptone broth and insulin stimulation. However, these results could be influenced by a lower urine volume in ulcer patients or in a correlation between the noradrenaline urinary levels and urine volume.

A Spearmen rank order correlation between the level of noradrenaline and urine volume revealed low positive correlations.

(a) Under basal conditions rho = +0·25
(b) After Peptone broth rho = +0·32
(c) After insulin rho = +0·18

None of these correlations even reached a 0·1 level of significance using a two-tailed test and all were too small to be considered of any consequence.

The fact that the ulcer patients tended to have lower urine volumes than the control subjects led to additional analysis being carried out based on an index of catechol output divided by urine volume. These analysis indicated that ulcer patients tended to excrete less noradrenaline per unit of urine than did the control subjects under all conditions. The differences were statistically significant, however, only after stimulation with Insulin.

(7) *Influence of environmental factors on catechol amine excretion.* The catechol collections were made under a variety of conditions which might have influenced catechol output. For example, the subjects were given psychological tests during the collection of the first hour basal samples and were intubated during collection of the second hour basal samples. Analyses failed to reveal any significant differences between Hour 1 and Hour 2 catechol output either on Day 1 or Day 2 for either ulcer or control subjects.

The possibility of a "novelty" or "first time" effect in Expt. 1 was examined in two ways. First, the catechol output of the first experimental day was compared with that of the second. These analyses revealed no difference between Day 1 and Day 2 with respect to noradrenaline excretion but indicated a significantly greater mean adrenaline output on the first than on the second day, both for the ulcer and control groups. Secondly, the catechol output of the first hour of the first experimental day was compared with the mean of the other three basal samples. Both ulcer and control subjects showed no significant difference with respect to rate of noradrenaline output but had significantly higher adrenaline rates during the first than during the subsequent three basal periods; in addition, both groups showed lower urine volumes during the first basal period than during the subsequent basal periods. The question to be considered is whether these indications of a "first-time" effect militate against the conclusion that ulcer subjects have lower noradrenaline excretory rates than do control subjects. One fact suggests that the answer is negative; in the experiment the noradrenaline output of ulcer subjects was found to be significantly lower than that of control subjects during the last three basal periods as well as during the first.

OL.
5
0/61

(8) *Reproducibility of catechol data in experiment.* Spearman correlation coefficients (SIEGEL, 1956) were computed to assess the similarity of the Hour 1 and Hour 2 catechol data.

The results indicated good reproducibility in the case of noradrenaline (rho values were +0·70, +0·58, +0·69 and +0·84) but poor reproducibility in the case of adrenaline (rho values were −0·02, +0·52, −0·21, and −0·01). To determine the reproducibility of the catechol data on two different days, the Hour 1 and Hour 2 data of Day 1 were summed and correlated with the summed data of Day 2. It was found that the control subjects had good reproducibility both with respect to epinephrine (rho = +0·67) and norepinephrine (rho = +0·60) but that the ulcer subjects had poor reproducibility both with respect to epinephrine (rho = +0·08) and norepinephrine (rho = +0·13).

It is interesting that there was good reproducibility in adrenaline and noradrenaline levels on Day 1 and Day 2 (for basal specimens) in the control subjects and poor reproducibility in the ulcer patients. It may be that the ulcer subjects response to the psychological testing during the first "basal" period on day 1 was responsible, however no definite evidence can be presented to support this.

The good reproducibility of noradrenaline levels when Hour 1 and Hour 2 are compared and the poor reproducibility of adrenaline levels may be more of an individually determined variable (a more consistent individual trait less influenced by external factors.)

Correlates of Catechol Amine Levels and Gastric Secretion

In the previous section the results of the various tests and measures were compared in ulcer patients and control subjects. Many of the differences between the two groups were highly significant and many of the pre-experimental hypothesis and predictions were supported.

The data was also considered in terms of the correlations of various measures to

the catechol amine levels and the correlates of gastric secretory levels regardless of whether the subject was an ulcer patient or a control subject.

Except for the predictions already stated (e.g. FTT and catechol amines) the data summarized in this section was not examined to test hypothesis which were formulated prior to the experiment. Rather, the data was examined in an exploratory fashion to determine new "leads" by *post hoc* review and interpretation of the data.

The data is presented in summary form since it can, at best, be considered as preliminary and suggestive.

There was another reason for examining the correlations of the various measures with the catechol amine levels and gastric secretion disregarding the ulcer/non-ulcer division. It was the feeling of the investigators that on the basis of the correlations of the measures with the presence or absence of an ulcer certain relationships with the catechols and gastric secretion would be "expected" and other relationships would not be expected. If these expectations were confirmed the data would carry a greater degree of certainty and more definitive hypothesis could be constructed.

(A) *Noradrenaline levels.* The "basal" noradrenaline levels (four basal periods combined) significantly correlated with the noradrenaline level obtained after insulin administration ($P = 0{\cdot}05$) but there was no correlation of the "basal" noradrenaline levels with the adrenaline level after insulin induced hypoglycemia.

The "basal" noradrenaline levels, the noradrenaline levels after insulin induced hypoglycemia and the mean value of all noradrenaline levels for each subject showed significant *negative* correlation with the "hyper" secretor score on the post experimental interview ("basal" levels $P = 0{\cdot}01$, after insulin $P = 0.05$ and mean value of all specimens $P = 0{\cdot}05$)

The "hyper" secretor scores on the psychological test battery (DAP, Saslow and Blacky) showed a negative correlation with the "basal" noradrenaline levels, level after insulin and mean value of all noradrenaline specimens. However, only the correlation with the post insulin level was significant at 0·05 level.

(B) *Adrenaline levels.* The "basal" adrenaline levels correlated with the adrenaline and noradrenaline levels after insulin hypoglycemia. The correlations were significant at the 0·05 level.

There was no correlation between the "basal" adrenaline level, the adrenaline level after insulin and the mean value of all adrenaline levels with the "hyper" secretor scores on the psychological test battery or the post experimental interview.

(C) *Gastric secretion.* As mentioned previously the mean volume and free acidity of the gastric secretion of the ulcer group was higher than that of the control group. However, there was considerable variation in each group and overlap between the groups so that there were no statistically significant differences.

The basal gastric secretion (Day 1 and 2 combined) showed a negative correlation with the combined basal noradrenaline level ($P = 0{\cdot}05$) and the mean value of all noradrenaline specimens ($P = 0{\cdot}05$). There was a negative correlation with the noradrenaline level after insulin but it was not statistically significant. ($-0{\cdot}27$)

The combined basal gastric secretion levels showed a negative correlation with the combined basal adrenaline level ($-0{\cdot}24$), adrenaline level after insulin ($-0{\cdot}21$) and the mean value of all adrenaline levels ($-0{\cdot}34$) but none of the correlations were statistically significant at the 0·05 level.

The gastric secretory levels after insulin and the mean value of all gastric secretory

VOL. 5 1960/6

levels showed no significant correlations with the combined basal adrenaline or noradrenaline levels, the adrenaline or noradrenaline values after insulin or the mean value of all adrenaline as noradrenaline levels. However, in all instances that gastric secretory levels and the noradrenaline levels had a negative correlation whereas there was considerable variation with the adrenaline levels.

The combined "basal" gastric secretory levels, the levels after insulin hypoglycemia and the mean value of all gastric secretory specimens did not significantly correlate with the scores on the FTT or the "hyper" secretor scores on the psychological test battery (DAP, Saslow and Blacky). However, the gastric secretory level after insulin and the mean value of all gastric specimens showed a positive correlation with the "hyper" secretor score on the psychological test battery that almost reached a 0·05 level of significance (+0·37 with +0·377 being necessary for $P = 0·05$).

The "hyper" secretor score on the post experimental interview was significantly correlated with all the gastric secretory levels. ("Basal" levels +0·47, after insulin +0·41 mean of all levels +0·45). The correlation was significant at the 0·05 level in all instances.

DISCUSSION

One conclusion arising from the investigations presented in this paper is that the ulcer patients have a lower noradrenaline excretion than do individuals without ulcers. Significant differences were found during "basal" conditions, after stimulation with peptone broth and insulin.

The psychological test battery assessed a series of psychologic "hyper" secretor and "hypo" secretor which had been described in the study by WEINER *et al.* (1957). These psychological factors identified the ulcer and non ulcer patient subjects at a statistically significant level. Furthermore, an interview conducted following the test procedures which also attempted to identify "hyper" and "hypo" secretor psychologic factors in relation to the test situation, was able to identify the ulcer and control subjects at a high level of significance. Perhaps, of more significance was the fact that the ratings on the post intubation interview correlated significantly with the actual gastric secretions, and was inversely correlated with noradrenaline levels.

Of further interest was the fact that the gastric secretory values did not show a significant difference in the ulcer and control groups. Although the mean values were higher in the ulcer group. The scores on the Focused Thematic Test correlated significantly with the total catechol amine output and the adrenaline percent during the test period but did not correlate catechol amine levels obtained in the other test periods. However, the FTT score did not discriminate the ulcer and control subjects.

The physiological and biochemical data was collected for the purpose of studying whether autonomic nervous system "balance" might be conceptualized by examining gastric secretory activity and urinary catechol excretion.

Although there is substantial evidence of a close correlation between the urinary excretion of catechol amine and sympathetic activity (VON EULER 1956) it does not seem justifiable to assume that the low noradrenaline output of the ulcer patients is an indisputable indication of low sympathetic activity. Some metabolic difference, such as activity of deaminating enzyme systems or the affects of other hormones could conceivably result in lower free catechol amine excretions in the urine of ulcer patients. However, pending some definite evidence of such mechanisms, the assumption that low catechol amine output in the urine of ulcer patients is indicative of low sympathetic activity seems warranted and helpful in expanding the approach to the problems of the control of gastric secretion in duodenal ulceration. It is not proposed that low sympathetic activity is the only disturbance of autonomic function underlying the ulcer diathesis. But rather that this is one aspect of a complex central nervous system dysfunction probably involving the hypothalamus and associated reflex centers.

This paper furthermore does not propose to delineate whether the psychodynamic, developmental and interpersonal factors are primarily responsible for the autonomic

inhibition or dysfunction which the data suggests. Furthermore, there is no evidence to suggest that the psychodynamic factors are the result of the autonomic dysfunction or other metabolic dysfunctions which may lead to the development or enhancement of "oral" needs or the reinforcement of conflicts in the oral area. All that can be definitively stated is that the data suggests that a relationship does exist between specific psychodynamic patterns and specific autonomic response characteristics (as reflected in a catechol amine levels.)

The results did strongly suggest that duodenal ulcer formation is related to low noradrenaline excretion. In addition, gastric secretion and acidity (at least during the "basal" periods) were inversely related to the noradrenaline excretion. These findings support the hypothesis of Waddell and others that gastric secretion is, in part, a function of gastric blood flow and to some extent may be controlled by the rate of transfer of water and ions from the blood vessels to the gastric lumen. This is further supported by evidence shown by WADDELL (1958) that gastric secretion can be arrested by the intravenous infusion of noradrenaline. Gastric blood flow appears to be an important factor in the etiology of duodenal ulcer yet there is a paucity of data on this topic.

The effect of removal of the pyloric antrum as a source of afferent impulses in reducing gastric secretion was briefly referred to in the introduction. Work by WADDELL has been undertaken to determine the possible role of the antrum in the control of gastric blood flow. It was demonstrated that antrectomy resulted in vasoconstriction of some of the gastric vessels. The antrum seems to function as a site of origin of visceral afferent impulses which influence the central reflex centers and the tonic discharges to the autonomic nervous system.

VOL.
5
1960/6

The multiple factors responsible for the basal secretion of the resting stomach have not been accurately defined. However, it has been shown that vagal integrity is important. There is general agreement that nervous influences account for a large part of the secretory activity of the empty stomach. WADDELL has described an unmistakable influence that the removal of the antrum has a pronounced affect upon basal secretion.

Although there is no certain proof, the observed changes in basal secretion produced by antrum excision seem consistent with the concept that the antrum is a source of afferent impulses which pass to central reflex centers and exert an effect upon the tonic state of such centers and the efferent discharge over parasympathetic pathways.

If non-ulcer subjects differ from ulcer subjects in the sensitivity of the antrum then one would expect that basal secretions and the secretion after peptone broth would differ from that of ulcer subjects as the non-antrectomized differed from those with their antrums removed. Since this evidence was not present in this study, sensitivity of the antrum did not appear to be the major difference which would account for susceptibility of one group to develop ulcers.

Histamine presumably exerts its affect directly upon the parietal cell of the stomach. Its stimulating action upon the output of acid in the stomach is potentiated by parasympathomimetic drugs. Most observers have found the secretory response to hisamine greatly reduced after vagatomy. WADDELL observed that antrum excision reduces or abolishes the ability of the gastric remnant to respond to histamine. The non-ulcer patients in this particular study did respond to histamine with secretion. The results of histamine stimulation again does not support antral sensitivity as the primary difference in the ulcer-non-ulcer group.

It would appear that the gastric secretion which occurs following insulin hypoglycemia is a result mainly of stimulation of the vagal centers of the brain, probably the hypothalamus. The effects of the stimulation of the hypothalamus are carried to the stomach over the parasympathetic pathways principally the vagus. Atropine, for example lessens or abolishes insulin stimulation. The available evidence indicates that cholinergic discharges from excitation of centrally placed para-sympathetic reflex centers are responsible for the gastric secretory effects of insulin.

The evidence from this experiment suggests that the main difference in the two groups, ulcer and non-ulcer, is a function of variations in tonic influences exerted on the reflex centers by the hypothalamus. It is interesting that the stimulus which primarily affects the effector side of the reflex (histamine) produced similar catechol amine and gastric secretory responses in both groups of subjects. While stimuli affecting the afferent side of the reflex (peptone broth)* or stimuli which involved the hypothalamus (insulin) highlighted the differences between the two groups. Actually the conclusions being drawn here are based on the fact that the difference in noradrenaline levels was possibly reflecting different levels of peripheral sympathetic activity.

It is hypothesized that the neurophysiologic difference between the two groups is not at the mucosal afferents, the neuro-effector or medullary levels, but probably at the hypothalamic level. The difference may involve a variation in the tonic inhibitory tone exerted by the hypothalamus on the medullary gastro-intestinal centres. Hence, if one stimulated the medullary reflex centers there might be no difference in sympathetic or parasympathetic reflexes in the two groups. This was suggested by the fact that the histamine produced a noradrenaline response which was equal in both groups. Insulin however, produced a considerably greater noradrenaline response in the non-ulcer group. (It is assumed that insulin is affecting primarily the hypothalamus while the central action of histamine has been described as stimulating medullary reflex areas.)

The hypoglycemia induced by the insulin is believed to lead to stimulation of posterior hypothalamus which further leads to peripheral sympathetic discharge as well as the activation of an adrenal medullary discharge. The fact that there was no great difference in the adrenaline levels but only a difference in the noradrenaline levels suggests the adrenal medulla and/or the sympathetic innervation of the adrenal medulla is not deficient or dysfunctioning. The evidence points to a dysfunction under certain conditions of the sympathetic fibres concerned directly with the activity or blood supply of the stomach.

The data from this experiment suggests that the concepts which were formulated by WEINER, REISER, THALER, and MIRSKY (1957) can be supplemented by the following information. The catechol amines are believed to be a reflection of the activity of the sympathetic nervous system as well as the adrenal medulla. Gastro-intestinal motor and secretory activity may be a result of neurogenic influences which includes a system of afferent fibers from the antral mucosa which go to the medullary reflex centers and the hypothalamus. The hypothalamus in turn may exert an inhibitory or facilitatory influence on the medullary reflexes. A decrease in the hypothalamic inhibition of medullary reflexes will lead to an increase in gastro intestinal reflexes and hence an increase in gastro-intestinal activity. Psychologic influences may affect the hypothalamus and alter its inhibitory or facillatory tone. On the other hand it may be that individuals who have a dysfunction of the hypothalamus not only display certain physiological differences in terms of gastric functioning but also display certain emotional and motoric behavioral differences. It may be that these differences are all contributed to by the central hypothalamic dysfunction (i.e. an hypothalamic imbalance may lead to the autonomic, physiologic, endocrinologic, behavioral, affective and psychodynamic correlates noted in patients with peptic ulcer.

* Stimulation of gastric secretion by peptone broth is not felt to be purely reflex, e.g. some feel peptone stimulates release of gastrin.

ENGEL (1958) pointed out that in the infant with a gastric fistula outgoing affects and increased motor activity were associated with the highest gastric secretory rates. It is interesting that in adults, active or overt expressions of aggression do not seem to be characteristic of individuals who develop duodenal ulcers. These findings are not contradictory. In a child one would expect a much more diffuse discharge from hypothalamic centers during states of activity which would include sympathetic and parasympathetic fibers. In adults aggressive motor behavior which was discharged to muscular channels might not be associated with gastro intestinal activity. The work of GASTAUT (1958) suggests that when cortical component of a conditioned response has been blocked either by drugs or by decortication then diffuse affective and autonomic components of conditioned response may predominate. Obviously part of a cortical response might be a motoric act. GASTAUT has pointed out that the caudal projections of the reticular system are inhibited when the rostral projections are activated. Hence, autonomic and affective responses associated with conditioning are inhibited when cortical motor responses are facillitated. If there is no performance of an aggressive act then the autonomic and affective components may be most prominant. The inhibition of motor conditioned reflexes or the voluntary learning of suppression of aggressive hebavior may show in humans as it does in cats, high amplitude, slow rhythms, in the unconditioned area during the process of inhibition. Further work in this area might be benefitted by the utilization of conditioning techniques in which gastric secretory responses were studied in conjunction with conditioned aggressive opperant behavior.

It is necessary to interpret the results of this project cautiously. Although certain relationships are strongly suggested by the data, there are many discrepancies and exceptions to even the statistically significant results. If a proper understanding of the psychophysiology of gastric secretions is to be developed these discrepancies must ultimately be explained. Perhaps the major area for caution involves the techniques and methods and the interpretations of the results. It must be recognized that even with the improvements in laboratory techniques, measurement errors are still considerable. The measurement of urinary catechol amines as an index of sympathetico adrenal responsivity is of course still open to many questions. In fact the whole significance of the urinary levels is far from clear. Although the particular assay method utilized in this study appears to be an accurate method of determining the presence of catechol amines in the specimen, the use of urinary specimens leaves many questions to be answered, among them the origin of catechol amines which are present in the urine. Furthermore, the levels noted cannot necessarily be taken to reflect the overall amount of catechol amines released in the body during a period of time. Even if most of the adrenaline and noradrenaline noted in the urine results from adrenal medullary and sympathetic nervous system activity, the effects of differences in adrenal clearance rates or differences in the metabolism of the catechol amines in different persons is still not clearly delineated. It would be of particular importance in establishing the mechanism involved in a psychophysiological chain of events to have available an accurate, rapid and sensitive measure which could detect changes in several parameters which are under investigation. If simultaneous measures of the changes in several parameters could be performed then the question of causality might be further clarified. Naturally a measure of urinary catechol amine levels representing the excretion over a one-hour period is far from ideal.

The utilization of catechol amine levels as an index of sympathetic nervous system activity or adrenal medullary responsivity merely compounds the problems already introduced by the questions raised by technique, questions raised about metabolism and questions about adrenal clearance of the catechols.

Furthermore, one must be extremely conservative in the theoretical assumptions

VOL.
5
1960/6

drawn from the data since the methods of evaluation of the psychologic factors are subject to many technical areas due to the inaccuracy of the techniques, as well as, the biases introduced by the experimenters. The utilization of definite criteria which were established prior to the reduction of the data; the complete independence of the functioning of the two teams of investigators certainly contributed to the significance of the findings. But it does little in helping us to understand the mechanisms and processes underlying the relationship of gastric secretory activity, catechol amin excretion and psychologic factors.

There were several obvious omissions in this study which leave several questions unanswered. For example, the inability to carry out measures of gastric motility was unfortunate. It is well recognized that the introduction of a new measure often introduces new variables into an experiment. Nevertheless recent developments have shown promise that new experimental tools may be forthcoming which may be admirably suited for studies such as the one described in this particular paper. In addition, the failure to measure pepsin secretion in the stomach or urinary or serum pepsinogen levels did not permit direct comparisons with the work of previous investigators, some of whose techniques and criteria were utilized in this study.

Although an attempt was made to structure the interviews in the psychological tests so that specific psychodynamic information could be obtained and reliable correlations between psychodynamic areas, catechol amines and gastric secretions carried out, the techniques available for the assessment of the behavioral and emotional information was far from satisfactory. Future approaches utilizing specific perceptual cures at liminal and subliminal levels together with classical and operant conditioning techniques may lend themselves amiably to more sophisticated studies allowing for a better delineation of the relationship of behavioral and emotional processes, to physiological activities and endocrinologic functions.

Many of the areas discussed in this paper may not appear related to psychiatric problems or even germane to psychosomatic areas. However, an effort has been made to relate only those findings pertinent to broadening the understanding of the psychophysiological influences on gastric functioning.

In spite of the voluminous literature on duodenal ulcer the pathophysiology is still not well defined and the mechanics of gastric physiological responses to emotional processes is even more vague.

This study does not attempt to do more than introduce another dimension which should be considered in understanding the translation of psychic processes into somatic changes. As our information regarding the complex physiological, endocrinological and neurophysiological interactions involved in gastric functioning expands, we can expect our abilities to more meaningfully and specifically utilize psychological techniques to assist our surgical and medical colleagues in the treatment of duodenal ulcer to improve.

OL.
5
0/61

SUMMARY

Gastric secretory studies and urinary assays for catechol amines were carried out on 10 patients with radiologically proven ulcers and 10 non-ulcer patients. A group of psychological tests and a specially constructed interview were administered. The patients whose psychological measures were scored (without any knowledge of clinical diagnosis, gastric secretion and urinary catechol amine levels) as demonstrating a high degree of anxiety and a low level of, or a discomfort with the expression of aggressive impulses were noted as being most likely to have a low noradrenaline output, and a duodenal ulcer.

The psychological measures discriminated ulcer and non-ulcer patients at a 0·01 level of confidence. Nor-adrenaline levels were lower in ulcer than non-ulcer patients.

The results reconfirmed the correlations previously noted in three types of studies: (1) The levels of adrenaline and noradrenaline excreted in a patient's urine correlates with the degree of aggressivity and anxiety expressed on specific psychological test measures; (2) Specific psychological characteristics can discriminate ulcer and

non-ulcer patients; (3) The ratio and level of urinary catechol amines may be a reflection of autonomic imbalance and are associated with duodenal ulcers.

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VOL.
5
1960/6

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OL.
5
0/61

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DISSOCIATION OF BEHAVIOURAL AND ELECTRO-ENCEPHALOGRAPHIC SLEEP IN TWO BROTHERS WITH *ENURESIS NOCTURNA**†

E. BENTAL, M.D.§

(*Received* 29 *July* 1960)

IN THE course of systematic electroencephalographic examinations of enuretic children, a most peculiar phenomenon was encountered. A distinct dissociation in the pattern of behavioural and electroencephalographic sleep was observed during an all-night electroencephalographic recording from two brothers, both enuretics.

Two brothers, born in 1942 and 1944, were referred to the Out-patient Department because of nocturnal enuresis and occasional day-wetting, from which they had suffered from their earliest childhood. The boys' parents are quite healthy. The children are boarders at a school for rabbinical studies, and bed-wetting each night, as well as occasional day-wetting, makes their life at school very unhappy.

The general physical and neurological examination revealed no abnormalities. Both boys are of small build and rather fat; both show slightly underdeveloped genitalia. X-ray of the lumbar vertebrae of both boys revealed a spina bifida in the region of the fourth and fifth lumbar vertebrae. Routine E.E.G. examinations showed both boys to have a slightly abnormal record with general irregular background activity, and random slow waves of the theta range.

Taking in consideration the boys' persistent nocturnal enuresis as well as the electroencephalographic findings, it was thought desirable to have an all-night E.E.G. in order to see whether any electroencephalographic changes could be observed at the time of the wetting during natural night-sleep.

METHODS

Recording was performed on two Grass Model IV, eight channel, electroencephalographs. Seven silver electrodes were applied to the scalp with collodium. Arrangement of electrodes is shown in Fig. (1a). One channel was connected to a special short-circuiting device, fixed in the beds, so that the wetting would be immediately indicated in the E.E.G. Both boys voided before going to bed at 10 p.m. They were put in separate, darkened rooms. External stimuli were eliminated as far as possible except for the noise of the recording itself. A physician and an E.E.G technician were in attendance throughout the night. In general, recording was performed at normal paper speed (30 mm/sec), certain parts were recorded at greater speed (60 mm/sec). Constant supervision, however, permitted immediate return to normal speed when any change in the record was noticed. Both boys fell deeply asleep in the course of one hour.

OBSERVATIONS

Recording was begun as soon as the boys went to bed, and was continued throughout the night. The waking record was performed with eyes open or closed according to the children's wishes. It showed a slightly irregular rhythm of 9 cycles/sec with random slow waves of the theta range (Fig. 1b, 1c.) Two hours later, although behaviourally the boys were quietly and deeply asleep, no change was to be seen in the

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VOL. 5 1960/6

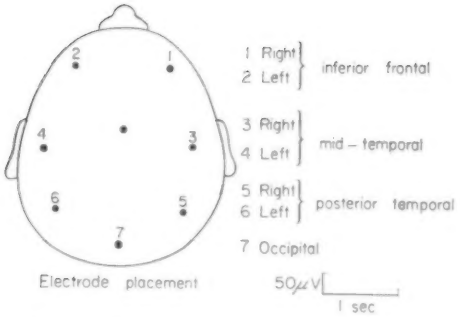

FIG. 1a: Placement of electrodes and calibration.

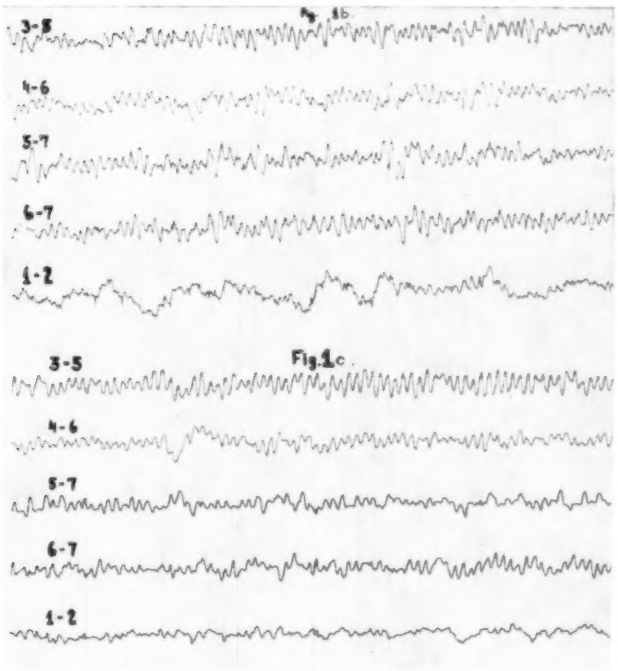

FIG. 1b: E.E.G. tracing of patient A., awake.
FIG. 1c: E.E.G. tracing of patient M., awake.

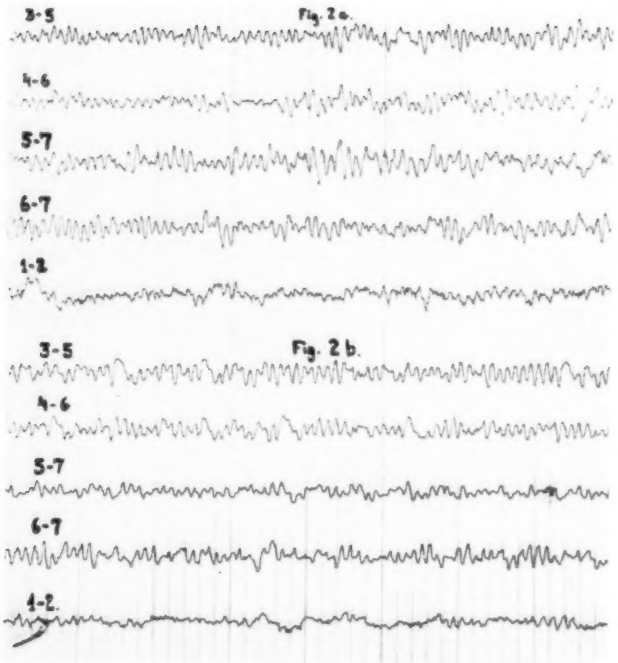

FIG. 2a: E.E.G. tracing with "Wake" pattern of patient A., asleep for 1½ hr.
FIG. 2b: E.E.G. tracing with "Wake" pattern of patient M., asleep for 3 hr.

VOL.
5
1960/6

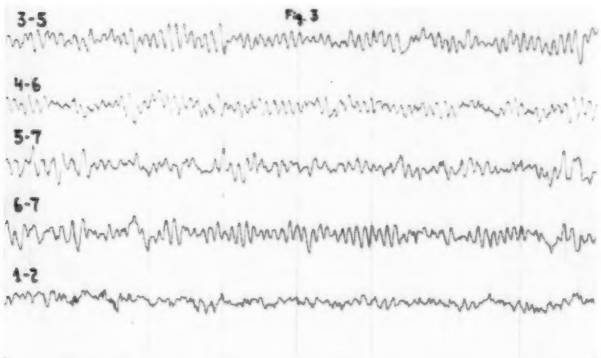

FIG. 3: E.E.G. tracing with "Wake" pattern of patient A., deep asleep at the time of wetting.

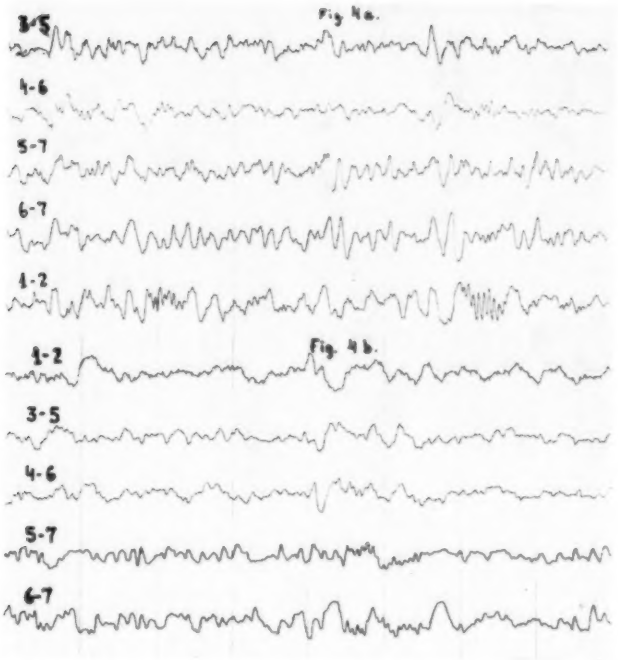

FIG. 4a: E.E.G. tracing of patient A., asleep after wetting showing spindles and slow waves of high voltage.
FIG. 4b: E.E.G. tracing of patient M., asleep after passage of urine showing spindles and random slow waves.

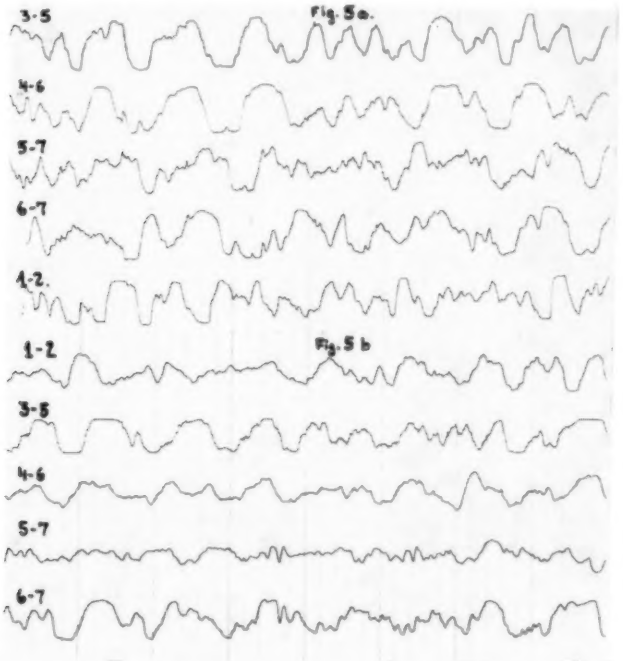

FIG. 5a: E.E.G. tracing of patient A., deeply asleep—slow and high voltage delta waves.
FIG. 5b: E.E.G. tracing of patient M., deeply asleep—slow and high voltage delta waves.

VOL.
5
1960/6

E.E.G. records (Fig. 2a, 2b). The typical stages of sleep records as described in the literature (BLAKE and GERARD, 1937; LOOMIS, HARVEY and HOBART, 1937; DAVIS, DAVIS, LOOMIS, HARVEY and HOBART, 1938; HENRY, 1941; GIBBS and GIBBS, 1950; KLEITMAN, 1950; MONNIER, 1952; SIMON and EMMONS, 1956) were not observed. Indeed, further recording during the night established the fact that both boys' waking and sleeping records remained almost identical. This E.E.G. pattern was recorded from the elder boy, M., until he woke up at 2.45 a.m. and asked to urinate. Even during that wakeful period no E.E.G. changes were recorded. While the younger child, A., was asleep, the same "wake" pattern was recorded. At 12.50 p.m. he spontaneously wet his bed without waking up, and without *any* change being recorded in the E.E.G. (Fig. 3). The boy continued sleeping quietly and deeply in a soaked bed. It was very difficult to arouse him in order to change the bed-clothes, a fact which indicated how deeply the child was asleep.

After the above-mentioned episodes both boys fell asleep again. At that time a completely different E.E.G. pattern appeared, with all the typical sleep-stages classically recorded in natural sleep: gradual disappearance of alpha activity, appearance of sleep spindles of 14 cycle/sec, and random delta waves then, finally, increase of delta waves in voltage and length (Fig. 4a, 4b, 5a, 5b). This pattern was continuously recorded until the early hours of the morning, when gradually, faster activity reappeared.

DISCUSSION

Ever since the classical investigations of electroencephalo-graphic sleep patterns it is well known that behavioural sleep is reflected electroencephalographically by typical patterns ranging from "scarce slow waves interfering with alpha rhythm of low voltage; slow rhythm of smaller voltage, intermingled with short spindles 14 cycles/sec; until there is a predominance of slow waves of high voltage" (MONNIER, 1952). These patterns develop in correlation with the different levels of sleep.

In the two cases reported here, we met the unusual phenomenon of dissociation of physiological and electroencephalographic sleep. In spite of the very deep physiological sleep—which is usually observed in enuretic children—the typical sleep patterns were not reflected in the E.E.G. during the pre-wetting period. During that time, the E.E.G. showed the same pattern as the "wake" pattern recorded before the children fell asleep.

VON ECONOMO (1929) in his classical description of encephalitis lethargica, and in his investigations of the problems of sleep, differentiated clinically between what he called "Hirnschlaf" and "Körperschlaf", i.e. "Brainsleep"' and "Body-sleep". In patients suffering from encephalitis lethargica he observed a disturbance of sleep function which manifested itself by extreme motor restlessness associated with deep "Brain-sleep", and vice-versa, complete motor relaxation, as appearing in physiological sleep, concomitant with acute cerebral alertness. It is worthy of note that a similar mechanism also seems to occur in somnambulism, the body being motorically alert while the brain remains deeply asleep. More recently an experimental dissociation of sleep has been shown to exist in dogs and cats poisoned by atropine, physostigmine or morphine; these animals were actually awake in spite of a sleep E.E.G. being recorded (WIKLER, 1952; BRADLEY and ELKES, 1953). KLEITMAN, who discusses the possibility of such a dissociation (DEMENT and KLEITMAN, 1957; KLEITMAN, 1957), mentions one case where a "wake" E.E.G. was seen while the subject was

unquestionably asleep, but dreaming. He concludes that behavioural sleep and the so called "sleep patterns" in the E.E.G. are not necessarily correlated. DITMAN and BLINN (1955) observed that in 20 adult enuretic subjects normal sleep patterns occurred up to 20 min or less before the wetting, and only then did a strong waking alpha activity appear.

In our subjects however a waking alpha activity was recorded for hours before the wetting or passing of urine. There can be no doubt as to the depth of the behavioural sleep of our two boys. A., especially, was very deeply asleep, since even the disturbing stimuli of the soaked bed did not wake him, while the "shaking-up" in order to arouse him and change the bed-clothes had to be very energetic. Of further interest is the fact that during the process of intentional awakening of A. and the spontaneous arousal of M., no electroencephalographic changes which might be indicative of electroencephalographic arousal (SCHMIDT, 1957) were observed, and the general electrical brain activity of both boys was almost identical, even during the wetting period.

The special interest of our cases lies in the fact that during the pre-wetting period of sleep the so-called "sleep patterns" were not observed. As soon, however, as one boy had woken up and consciously asked to urinate, and the second one had passed urine without waking up at all, a complete parallelism of behavioural and electroencephalographic sleep took place. In the light of this observation, there is reason to assume that in human beings the volitional factor plays an important role, even subconsciously, in inhibiting electroencephalographic sleep. The resulting dissociation of sleep might thus be explained on a broad psycho-physiological basis. It is most probable that children, who experience the personal and social unpleasantness of bed-wetting, develop a strong "will" to keep awake in order to avoid this disturbing event. This "will" seems to be reflected in the E.E.G. so that its pattern remains "alert" although the children show all the manifestations of deep physiological sleep. After both boys had passed urine their E.E.G. patterns became typical "sleep" ones because this unconscious "will", which had been the cause of the dissociation, ceased to exist. Thus the phenomenon described above seems to indicate the influence of psychological factors on the electrical activity of the brain.

VOL.
5
1960/6

SUMMARY

A dissociation of sleep was observed in two enuretic brothers during the pre-wetting period while, after the wetting, absolute parallelism between physiological and electroencephalographic sleep was noted.

An attempt was made to explain this phenomenon on the basis of the volitional factor present in growing-up enuretic children who, suffering severely from their handicap, try to keep alert during sleep in order to avoid wetting. This assumption would indicate the influence of psychological factors on the electrical activity of the brain.

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OL.
5
0/61

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BEHAVIOURAL CORRELATES OF GENETICALLY ENHANCED SUSCEPTIBILITY TO STOMACH LESION DEVELOPMENT*

J. O. SINES†

(*Received* 13 *June* 1960)

IN AN earlier paper (SINES, 1959) data were presented regarding the increased susceptibility to stress induced stomach lesions in the rat following selective breeding for two generations. In that earlier study it was noted that animals which developed stomach lesions appeared to squeal more upon handling, and to resist handling more vigorously than stock animals. Such findings suggested that selection pressure relative to the particular stress response of stomach lesion development might result also in discriminable behavioural changes which could be measured by means of standard observational techniques.

The present report deals with objective behavioural data and lesion incidence among stock Sprague-Dawley albino rats and the S_3,S_4, and S_5 generations of animals selectively bred for stomach lesion development.

VOL.
5
1960/6

METHOD

Subjects

Subjects (Ss) in this study were 145 rats all of which were 80–90 days of age when subjected to the stress experience. The groups of animals used are indicated in Table 1. All animals were born and raised in this laboratory and had been maintained on standard laboratory regime which involved *ad lib* food and water, individual housing for pregnant and nursing females, group housing after weaning at 21 days of age, laboratory temperature controlled at 74 $\pm$ 2°F, and a 12 hr light-dark cycle.

TABLE 1.—NUMBER OF ANIMALS IN EACH OF THE GROUPS USED IN THIS STUDY

Group	*N* Males	*N* Females	*N* Total
Sprague-Dawley	20	22	42
S_3	26	31	57
S_4	17	13	30
S_5	9	7	16
	72	73	145

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† From the Washington University School of Medicine.

Apparatus and procedure

Between 80 and 90 days of age all Ss were observed individually for a 2 min period in 5 × 3 feet open field, the floor of which was marked off into 1 × 1 foot squares Behaviour noted in the field consisted of number of squares entered, number of times each animal reared on its hind legs and number of boluses deposited. The first two measures, number of squares entered and amount of rearing are used as indicators of activity and the number of boluses is conventionally employed as a measure of emotionality in the rat. Within 12 hr of the open field experience, all animals were individually placed for 12 hr in a wire mesh enclosure which effectively immobilized the animal. Immobilization for 12 hr was employed with subjects on which the present report is based while previously 48 or 24 hr of immobilization in a plaster of paris cocoon had been used. Forty eight and twenty four hours of plaster cast immobilization were found to produce stomach lesions in 100 per cent of S_3 animals, necessitating the reduction in the severity of the imposed stress in order to allow for continued selection. S_5 animals were injected with an amount of an anticholinergic compound sufficient to prevent lesion development in stock animals immobilized for 12 hr (SINES, 1960).

Following the 12 hr period of immobilization animals were anesthetized with ether and the stomachs inspected for the presence of lesions. Stomachs were rated 0–4 depending upon lesion severity, with "0" indicating a normal stomach; "1" small petechiae; "2" irregularity of the mucosal lining; "3" a clearly defined defect which usually involved bleeding; and "4" the most severe lesion observed, being a palpable defect which almost invariably included considerable congealed blood in the base of the crater.

Selection procedure

Three females and two males of the S_3 group showing severe bleeding lesions were saved for breeding and were the parents of the S_4 subjects. One S_4 male and two S_4 females were saved for breeding purposes. Since all S_4 animals showed lesions, the breeding stock from that generation was selected on the basis of lesion severity. Those S_4 animals which were saved had lesion with ratings of "4". The one S_5 male and the four S_5 females which were saved for breeding were those with lesions with ratings of "4". S_6 animals have not yet been subjected to stress.

RESULTS

Stomach lesions

As noted in several previous reports (SAWREY, 1957; SINES, 1959) females in all of the groups showed higher incidence or severity of stress-induced stomach lesions. The difference between stomach lesion incidence in stock males and females was significant beyond the 0·01 level, although the differences between males and females in the other groups did not reach a significant level. In the S_4 generation, where incidence was 100 per cent in both males and females, the *severity* of stomach lesions was greater for females, although the difference in severity did not reach statistical significance.

From Table 2 it can be seen that the incidence of stress induced stomach lesions continued to increase through the S_4 generation. The data relative to lesion incidence in the S_5 animals are not comparable to the S_3 and S_4 data because prior to immobilization the S_5 rats had been given an anticholinergic drug in order to reduce the number

TABLE 2.—STOMACH LESION INCIDENCE IN FOUR GROUPS OF ANIMALS

Group	Males		Females		Sex difference	Significance of sex difference
	Lesion incidence	P*	Lesion incidence	P*		
Sprague-Dawley	20%	—	45%	—	+25%	<0·01
S_3	71%	<0·01	82%	<0·01	+11%	NS
S_4	100%	<0·01	100%	<0·01	0%	NS
S_5	25%	<0·05†	45%	<0·01†	+20%	NS

* Significance of comparison with Sprague-Dawley.
† Significance of comparison with Sprague-Dawley animals premedicated with 0·17 mg/kg of Probanthine (registered brand name) where lesion incidence was 0%.

and severity of lesions. Stock animals so treated with an anticholeinergic before 12 hr of immobilization do not develop stomach lesions. These data add further support to the original data on which was based the conclusion that there is a significant genetic factor determining an organism's predisposition to develop acute ulcerative stomach lesions following immobilization induced stress.

Weight

The data found here concerning body weight agree, in general, with the trends observed in other inbred strains in that the average body weights in the S_3, S_4, and S_5 generations of lesion susceptible animals (both males and females) were significantly smaller than the original stock from which they were drawn. Of particular interest however, was the tendency, first seen in the S_4 females and clearly present in both males and females of the S_5 generation, for weight to regress toward the mean weight of the stock animals (see Table 3).

In another study in this laboratory of several pure strains of the laboratory rat, the rank order coefficient of correlation between mean weight and number of generations of brother by sister mating was found to be −0·90. In view of such data the postulation of any relationship between weight and susceptibility to stomach lesion development seems unwarranted at this point.

TABLE 3.—COMPARISON OF MEAN BODY WEIGHT (IN GRAMS) OF FOUR GROUPS OF ANIMALS

Group	Males		Females		Sex difference	Significance of sex difference
	Weight	P*	Weight	P*		
Sprague-Dawley	324·6	—	203·1	—	121·5	<0·01
S_3	268·4	<0·01	169·8	<0·01	98·6	<0·01
S_4	259·2	<0·01	176·9	<0·01	82·3	<0·01
S_5	268·9	<0·01	191·0	<0·01	77·9	<0·01

* Significance of comparison with Sprague-Dawley.

VOL. 5 1960/6

The differences between mean weights of the males and females were statistically highly significant in each group although the magnitude of the difference decreased regularly.

Open field behaviour (*summarized in Table* 4)

Number of squares entered. Although S_3 and S_4 males entered a significantly greater average number of squares in the open field than did stock males, the average number of squares entered by the S_5 animals was not statistically different from that

TABLE 4.—COMPARISON OF SPRAGUE-DAWLEY AND LESION SUSCEPTIBLE ANIMALS ON OPEN FIELD BEHAVIOUR

Group	Males		Females		Sex differences†	Significance of sex differences
	Squares	*P**	Squares	*P**		
Sprague-Dawley	19·0	—	28·6	—	−9·6	<0·05
S_3	25·3	<0·05	32·1	NS	−6·8	<0·01
S_4	29·1	<0·01	31·8	NS	−2·7	NS
S_5	22·4	NS	24·1	NS	−1·7	NS
	Rearing	*P**	Rearing	*P**		
Sprague-Dawley	7·0	—	10·4	—	−3·4	<0·01
S_3	10·7	<0·01	12·8	<0·05	−2·1	<0·01
S_4	13·1	<0·01	11·8	NS	+1·3	NS
S_5	9·1	<0·10	11·9	NS	−2·8	<0·05
	Defecation	*P**	Defecation	*P**		
Sprague-Dawley	2·0	—	0·6	—	+1·4	NS
S_3	4·7	<0·01	3·0	<0·01	+1·7	NS
S_4	4·8	<0·01	2·3	<0·05	+2·5	<0·05
S_5	3·1	NS	3·1	<0·01	0·0	NS

* Significance of comparison with Sprague-Dawley values.
† Plus signs indicate higher mean scores for males.

of stock males. This regression by the S_5 males toward the mean number of squares entered by the stock males paralleled the similar but smaller trend noted above in body weight.

Among females, the average numbers of squares entered by the third, fourth, and fifth generations of lesion susceptible animals were not significantly different from the average of the female stock animals. The average number of squares entered by the S_5 females was lower than the female stock value (not significant) but it was significantly lower than the female S_3 average (0·01 level of significance).

Rearing. The average amount of rearing in the open field by S_3 and S_4 males was

significantly greater than the average amount of rearing done by the stock males. Here again, however, the regression toward stock levels by the S_5 animals was noted.

Although the S_3 females reared more often in the open field than stock females, (0·05 level), the S_4 and S_5 females regressed slightly to levels not significantly different from the mean of the stock females.

In the present study both of the above measures, number of squares entered and amount of rearing, were considered to be measures of gross motor activity. Thus, as can be noted in Table 3, successive selectively bred generations of lesion susceptible animals tended to manifest increased activity when subjected to the novel, mildly stressful open field situation. The tendency for higher levels of motor activity to characterize those animals more susceptible to stomach lesion developments is further supported by the sex differences where it was found that females tended to manifest both higher activity levels and higher lesion incidence.

Defecation. With regard to defecation, as was the general case with the activity measures, the third and fourth generation susceptible males showed significantly higher mean scores, while the mean for the S_5 group was not significantly larger than the stock animals mean scores.

There was, among all three generations of lesion susceptible females tested, significantly more defecation than the stock animals showed.

Litter size and delivery among lesion susceptible animals

During the two and one half year period in which this research has been under way, stock animals have been bred and raised in this laboratory in order to ensure a population of stock animals with pre-stress experimental backgrounds as similar as possible to those of the selectively bred animals. Although records have not been kept systematically, the average litter size for stock animals has been between 8 and 12 pups, with the range of from 6 to 17. None of the stock females have died in labor or in delivery.

The average litter size in the S_3, S_4 and S_5 generations has tended to be smaller, 5·7, 5·0, 7·0 respectively. Whether the differences between stock and the experimental animals in mean litter size are statistically significant cannot be determined at this point. The trend noted, however, suggests that there are other basic characteristics also in which stock animals may differ from animals which are susceptible to stress induced stomach lesions.

The frequency with which females of the selectively bred generations have died in labor or during the delivery of their pups has been striking. Two of the S_2 females died while delivering their third litters, at approximately 280 days of age. One S_3 female died delivering her second litter at approximately 210 days of age and a second S_3 female died during the delivery of her third litter when she was about 280 days of age. At the age of 280 days the stock females in this laboratory have been able to deliver litters of average size with no apparent difficulty. Neither of the two S_4 females appeared to have serious trouble in delivery but to date, two of four S_5 females have died during delivery.

Another observation involves the tendency for lesion-susceptible females, which do deliver their pups, to ignore their young. The causes for such non-maternal behavior are not clear at this time but may have specific significance in view of some of Cannon's work (quoted in BEST and TAYLOR, 1945, p. 945). Cannon found that

"kittens deprived of their sympathetic trunks grow normally, female cats become pregnant and give birth to young, though *the mammary glands do not function and the maternal instinct is lacking*" (present authors' italics).

It may be that the selection pressure here employed has resulted in animals which are, to some degree, functionally "sympathectomized". Such is our present working hypothesis developed to accommodate the data reported here, Cannon's findings, and data we have reported elsewhere (SINES, 1960) relative to drug effects on lesion incidence in rats.

Finally, one of the S_4 females was in labor for over 8 hr with her second litter and appeared close to death when her pups were delivered surgically. She was found to have 8 fetuses, only 4 of them fully developed. On the basis of these additional unsystematic observations, further studies of the pregnancies and deliveries will be made.

DISCUSSION

The data presented here lend support to a preliminary observation that rats which develop stomach lesions following the stress of immobilization are more active and emotional. Further, successive generations of animals selectively bred for lesion development were significantly smaller in body weight than the stock from which they were originally drawn.

The tendency for the S_4 and S_5 generations to regress toward the stock animals in almost all of the above characteristics may be the result of the selection procedures employed, particularly with S_4 animals. The fact that 100 per cent of the S_4 animals demonstrated stomach lesions made it necessary to select breeding stock from that group on the basis of lesion severity, a criterion which was without doubt less discriminating than an all-or-none criterion. For that reason the use of anticholinergics to retard lesion development among the susceptible animals was begun with the S_5 animals. The assumption was made that only highly susceptible animals would develop stomach lesions under stress if an appropriate amount of a drug which is specific for the control of stomach lesions has been used. Data supporting the use of anticholinergics to control stress induced stomach lesions in the rat have been presented elsewhere (SINES, 1960).

The striking tendency for lesion susceptible females to cast smaller litters and to have an unusually high fatality rate during delivery was unexpected and is to be studied closely in future generations. Attention is also presently being directed toward the study of other characteristics such as the probably differences in physiological response patterns and possible differences in learning ability between lesion susceptible and stock animals; characteristics in which there may also be changes as a result of the sort of selection pressure used.

On the basis of the data presented above one may state that animals, of this species at least, which develop stomach lesions when exposed to a given amount of stress differ from others which do not develop stomach lesions when subjected to objectively identical amounts of stress in that the former animals:

(1) show more spontaneous exploratory activity in a novel situation, (number of squares entered and amount of rearing in the open field)

(2) are more emotional in response to a novel situation (defecation in the open field)

(3) tend to produce smaller litters

(4) are offspring of females which both: (a) have greater difficulty delivering live pups and (b) fail more often to mother the pups which are born.

SUMMARY

Data are presented which indicate that the S_3, S_4, and S_5 generations of rats, selectively bred for susceptibility to stress-induced stomach lesions, are significantly lighter in body weight as well as more active and more "emotional" in an open field situation than are randomly selected Sprague-Dawley albinos. The selection procedures employed have continued to result in greater incidence of stress induced stomach lesions although a tendency was noted for the S_4 and S_5 animals to regress toward the levels of stock animals in some of the behavioural characteristics studied. There appears to be a tendency for the stomach-lesion susceptible females to cast smaller litters and therefore to be an unusually high proportion of lesion susceptible females to die during delivery. The tendency noted for lesion susceptible females to ignore their pups may be related to Cannon's earlier work on sympathectomized animals. A number of leads which require continued study were mentioned.

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VOL.
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1960/6

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AN EXPERIMENTAL TEST OF THE PERMANENCE OF LEARNING DEFICITS IN THE ENVIRONMENTALLY RESTRICTED RAT*†

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A NUMBER of studies have indicated that a variety of early experiences which differ from the standard environment of a laboratory cage enhance the learning ability of the rat in later life (FORGAYS, 1952; HYMOVITCH, 1952; BERNSTEIN, 1952; LEVINE, 1956; LEVINE, 1956; WEININGER, 1956; and BERNSTEIN, 1957). FORGAYS and FORGAYS (1952) compared rats reared in special free environments with those reared in restricted environments. The free-environmental animals were found to be significantly superior as measured by a modification (RABINOVITCH, 1949) of the HEBBS-WILLIAMS test (1946). Because the superiority was maintained in two consecutive series of the same tests, the authors considered the effects to be permanent. HYMOVITCH (1952) reported that rats reared in a free environment were superior in the HEBBS-WILLIAMS test to those restricted to stovepipe cages but he found no difference between the two groups using an enclosed T-maze. He postulated that enriched early experience affected problem solving, but not rote learning. He concluded that the superiority of the free-environmental animals was "relatively permanent and possibly irreversible." THOMPSON (1954) has cited these studies as evidence that " . . . the amount of variance that can be produced in rat intelligence by altering environment is almost as much as can be obtained by selective breeding for brightness and dullness."

Since practice is a variable which may compensate for the initial inferior performance of restricted animals, one would predict that the amount of practice involved in a given learning test would affect the permanence of the retardation of the restricted animals. To test this hypothesis we have used human handling as environmental enrichment and two learning tests which differ markedly in amount of practice involved.

METHOD

Twenty male albino rats of the Wistar strain were assigned at random to one of two groups on the twentieth day of life. Then each animal of one group (experimental) was handled individually by the same person for 10 min per day, at the same time of day, five days per week, for 3 weeks. Handling consisted of holding the animal in one hand and stroking it repeatedly with the other hand from head to tail, with the

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animal facing the experimenter. Animals of the second group (control) were never touched after being placed in cages on the twentieth day of life.

Animals were housed individually in wire cages arranged in racks so that handled and unhandled animals alternated, and with equal numbers of each group at each level in the rack. A diet of Purina Laboratory Chow and drinking water were available *ad libitum*, except that during the discrimination learning tests, each animal was permitted to eat only one hour per day immediately after the tests. The temperature of the animal room was maintained 80 $\pm$ 2°F.

After three weeks the animals of each group were tested on a black-white discrimination problem. The apparatus was a T-shaped discrimination box, described in detail elsewhere (Bernstein, 1957). Either arm of the T could be lighted, and the training was light-positive. The sequence of left and right turns for the lighted alley was LRRLLRLRRL for the odd tens of trials and RLLRRLRLLR for the even tens. Animals were allowed 5 runs a day for the first 2 days and 10 runs a day thereafter, until each animal reached the criterion of learning (2 successive errorless days of 10 trials each). All animals were given at least 100 trials. Record was also kept of the number of errors made by each animal. An error was considered to have been made if the animal's body, exclusive of the tail, entered the unlighted T-arm.

When all animals completed the discrimination tests they were tested by a shock-escape learning problem. The apparatus for the test consisted of a wooden box with a glass front and a grid floor. The box was 47$\frac{1}{4}$ in. long, 7 in. wide, and 18 in. high. The grid floor was 37$\frac{3}{4}$ in. long. The grid was constructed of $\frac{1}{8}$ in. diameter steel bars spaced $\frac{3}{4}$ in. apart. A continuous 60 cycle square wave shock was supplied to the grid by an Applegate Model 228 stimulator, set at 250 DC microamperes. An interval relay served to alternate the current so that every other bar of the grid was charged every other second. A flat plexiglass plate, 4$\frac{1}{4}$ in. by 4$\frac{3}{4}$ in., was fitted over the center of the grid. Each animal was given five 1-min trials, and was introduced at opposite ends of the apparatus on alternate trials. During each 1-min trial the animal was free to move about on the grid or remain on the plexiglass plate, where it escaped the electric shock. The measure of learning was the time spent on the escape plate during the 5 trials.

One month after all animals had completed the tests on both shock-escape and discrimination problems, they were retested on the same tasks. One month from the completion of the second learning trials they were tested for the third time.

All data were analyzed by the Mann-Whitney *U* Test (SIEGEL, 1956). This is the most powerful non-parametric analogue of the *t*-test.

RESULTS

Table 1 summarizes the data for the discrimination problem learning. In the first test the handled animals required fewer trials and made fewer errors to reach the criterion of learning than did the unhandled ones. The differences were highly significant ($P = 0{\cdot}01$ and $0{\cdot}001$). When the test was repeated a month later both groups of animals showed an improvement in their performance by reaching the criterion of learning with fewer trials and making fewer errors. However, the superiority of the handled group persisted as shown by significantly fewer trials necessary to reach criterion of learning ($P = 0{\cdot}02$) and fewer errors ($P = 0{\cdot}05$). The third test is especially noteworthy. Whereas both groups showed continued

decrease in trials necessary to reach the learning criteria and in errors committed, the unhandled animals made greater improvement and equalled the performance of the previously superior handled group.

Table 2 summarizes the results of the shock-escape learning tests. The handled animals showed a significant ($P = 0{\cdot}02$) superiority in the first test. In the two

TABLE 1.—DIFFERENCES BETWEEN HANDLED AND UNHANDLED ANIMALS ON DISCRIMINATION LEARNING TEST

		Handled	Unhandled	P*
First Test	Mean no. of trials to reach criterion	123·0	159·0	0·01
	Mean no. of errors for first 100 trials	32·4	47·0	0·001
Second Test	Mean no. of trials to reach criterion	104·0	143·0	0·02
	Mean no. of errors for first 100 trials	13·8	19·3	0·05
Third Test	Mean no. of trials to reach criterion	83·0	88·0	0·33
	Mean no. of errors for first 100 trials	12·0	13·0	0·26

* Significance of difference between handled and unhandled animals.

TABLE 2.—MEAN TIME IN SECONDS ON SAFE AREA IN SHOCK-ESCAPE APPARATUS

	1	2	3	4	5	Total time	P*
First Test—Handled	13·5	29·6	23·7	33·0	19·4	119·2	0·02
Unhandled	5·3	9·5	15·3	15·3	21·0	60·2	
Second Test—Handled	24·5	32·9	13·5	29·4	23·8	124·4	0·01
Unhandled	11·7	8·8	6·8	8·9	6·3	42·5	
Third Test—Handled	29·6	24·0	30·3	35·1	37·0	156·0	0·05
Unhandled	12·2	16·6	11·1	18·2	10·1	68·2	

* Significance of difference between handled and unhandled animals.

succeeding tests the handled animals showed a steady improvement while the unhandled animals did worse in the second testing, and in their third test improved only to the level of the first testing.

DISCUSSION

Our findings with the discrimination learning tests indicate that the effects of restricted early experience are temporary, given a sufficient amount of practice. FORGAYS and FORGAYS (1952) found that the superiority of their enriched environment

animals persisted in their second series of tests and concluded that the differences were permanent. Our results in the first and second series of discrimination learning tests were similar to those of FORGAYS and FORGAYS. Had we terminated our experiment at that point, we might have concluded that the effects were permanent. However, the rates of improvement between the second and third series of tests showed such a marked difference in favor of the unhandled group (13·0 per cent for the handled animals, and 32·6 per cent for the unhandled) that the performance of the unhandled group equalled that of the handled group.

In the shock-escape learning tests the superiority of the handled over the unhandled animals persisted throughout the three test periods. This may be accounted for by the nature of the task. The rats were exposed to only a 5-trial learning situation of a painful nature, as compared with the hundred-or-more trials on the discrimination learning task.

The findings on the whole are consistent with the hypothesis that the effects of early restriction on learning are overcome or compensated for by sufficient opportunity for practice. It would appear that the permanence of the effects of early restriction on later learning is not an all-or-none affair. Under certain conditions the effects are reversible. Our findings suggest that the amount of practice is one of these conditions.

SUMMARY

Twenty Wistar albino rats served as subjects in a study designed to determine whether an enriched early environment (human handling) would produce permanent effects on learning of two selected tasks. From the age of 20 days the experimental animals were handled individually for 10 min per day, 5 days per week, for 3 weeks. Control animals were never touched after their original placement in cages on the twentieth day of life. Following the handling period, both groups were tested on a discrimination problem requiring a large number (100–200) of trials and on a 5-trial shock-escape learning problem. All animals were retested one month after the completion of the first learning trials. A third testing followed one month after completion of the second learning trials.

In the discrimination learning, the handled animals were clearly superior in the first learning trials and the difference persisted in the second learning trials. In the third series of tests the unhandled animals caught up with the handled group by achieving a greater degree of improvement in performance. In the shock-escape learning, the handled animals remained significantly superior throughout the 3 series of trials. The handled animals showed steady improvement, whereas the unhandled failed to improve.

It is postulated that the difference between the findings on the discrimination learning and the shock-escape learning was due to the much greater opportunity for practice in the discrimination problem as compared with the shock-escape problem. It is suggested that the permanence of effects of early restriction on later learning is not an all-or-none affair, and that the effects may be reversible under certain conditions. Our findings indicate that opportunity for sufficient practice is one of these conditions.

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THE COMPREHENSIVE TREATMENT OF BRONCHIAL ASTHMA FROM THE STANDPOINT OF CORTICOVISCERAL PATHOLOGY

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INTRODUCTION

THERE are few physiological functions of the organism the nervous regulation of which has been studied as thoroughly as the function of breathing, and there are few medical diseases where it has so definitely been proved that disorders of nervous regulation play a decisive role in their development as is the case with bronchial asthma. Nevertheless, the complicated relationships within the neuro-humoral regulatory mechanisms are not always taken into account in the treatment of bronchial asthma, and the therapy often follows two extremely one-sided directions: anti-allergy treatment in the narrow sense of the word is directed almost entirely towards the humoral sphere (autovaccines, antihistamines etc.), whereas psychosomatic medicine often only deals with the psychic, emotional aspect of the whole illness (e.g. EDGELL 1955, CARBALLO 1958): in numerous psychoanalytic studies the emotional life is even reduced to the sexual sphere (e.g. STEIN and OTTENBERG 1956).

The classical anti-asthmatic pharmaco-therapy (adrenaline, ephedrine), which acts directly on the central nervous regulation, is currently used in large doses generally in the treatment of the acute state, and has not become the basis of a rational therapy of the chronic illness. On the contrary, it is well known that drastic treatment by an overdose of adrenaline or its homologues inductively produces an even worse state, after a short period of improvement. The antagonistic effect of small and large doses of adrenaline on different systems (vessels, muscles) has also been shown experimentally (YERMAKOV 1954).

Starting from the theoretical principles and experimental facts of corticovisceral physiology and pathology elaborated in the first place by BYKOV (1947) and others, an analysis of the central nervous patho-physiological mechanisms underlying the development of bronchial asthma was attempted. A method of treatment based on this analysis was developed. Two different, but mutually related disturbances of the CNS play a decisive role in the formation of the spastic disposition: a pathologically increased excitability within a functionally limited region of the CNS, the so-called inert point of excitation (PAVLOV, 1934) or expressed in a different way by UKHTOMSKY (1926) a pathological dominant; and secondly, a general weakening of the cerebral cortex.

In the case of bronchial asthma the pathological dominant is formed in the region of the vagal centres as a result of the repeated "bombardment" of these centres by afferent impulses. Whether these impulses come from the interoceptors of the respiratory tract (as in chronic bronchitis, or from working in a dusty environment) or by

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VOL.
5
1960/6

way of chemo-receptors due to the effect of specific allergens is not so important. According to the laws of the dominant, (UKHTOMSKY 1926) which like a magnet attracts all impulses coming into the CNS, indifferent agents of the most varied types—intero-ceptive, extero-ceptive or psychic—then evoke typical spastic states. When attempting to explain more fully the development of the pathological dominant, at first sight it appears that it is formed primarily in the subcortical centres, because it is well known that normally autonomic reflexes are integrated primarily at this level. Physiological experiments and clinical experience, however, have proved that the problem is more complicated. The results of experiments in which either interoceptive or presensory–extero-ceptive conditioned reflexes, (which have a analogous course) have been elaborated (AYRAPETIANTS 1949; BYKOV and PSHONIK 1945; LOBANOVA and FELBERBAUM 1951; PSHONIK 1949), allow the conclusion to be drawn that the inert point probably only arises when the impulses "penetrate" from the subcortical region into the cerebral cortex. In the above mentioned experiments it was shown that the unconditioned stimuli (which also include the interoceptive stimuli) are extinguished if repeatedly applied alone, and that only by the frequent association with conditioned stimuli, i.e. by connecting up a reflex arc in the cerebral cortex, is a conditioned reflex formed. All this led BYKOV and his co-workers, to the conception that the pathological inert point is produced in a similar way. "The pathological process of the internal organ" they write "begins to send intense afferent impulses to the CNS, which sometimes penetrate into the cortex. Gradually an inert point is formed in the cortex where particularly these impulses are perceived. . . . " (BYKOV and PSHONIK, 1949).

Clinical and experimental findings further showed that the pathological inert point nearly always arises on the basis of a weakened cerebral cortex (TATARENKO 1951; PETROVA 1946, and others). It is well recognized that stimuli from the continually changing external milieu are integrated primarily in the cortex, whereas impulses from the internal organs are inductively inhibited and for this reason also not perceived. The functional weakness of the higher levels of the CNS, which may arise from the most varied causes (infection, fatigue, psychic traumatisation, etc.) becomes the soil for the "penetration" of interoceptive impulses in the cortical sphere and for the formation of the pathological dominant. This view helps us to understand why a spastic disposition does not arise in all persons who suffer from chronic bronchitis, or who work for years in a dusty milieu, and conversely why even the severest psychic traumatisation does not necessarily become the stimulus for the development of bronchial asthma. It is the association of both pathogenic factors, i.e. primary damage of the respiratory tract (or allergic sensitization) with simultaneous weakening of the regulatory function of the cerebral cortex, which leads to the development of the asthmatic syndrome.

All this suggests that the therapy of bronchial asthma must be comprehensive and that an attempt must be made to influence all links of the pathogenic chain:

(1) It is necessary to prevent the inflow of irritant impulses from the periphery or to reduce it as much as possible.
(2) It is necessary to suppress the pathological dominant and ideally to extinguish it.
(3) It is necessary to increase the functional tonus of the higher parts of the CNS.

PROCEDURE AND RESULTS

Independently of whether the bronchial asthma has been evoked by physical, chemical or other irritant stimuli, inflammatory processes of the respiratory pathways

almost always develop and treatment is therefore started by "cleaning the terrain" with the help of radical antibiotic and antiphlogistic treatment. ("Stoss" therapy). The appropriate antibiotic is given for approximately one week, and then salicylates are given for at least a further week. We give acetylsalicylic acid (three or more times daily in 1·0 g doses) in combination with *ephetonin* (0·01 g or more per dose) and small doses of Luminal. In this way the disposition to spasticity is often considerably decreased from the beginning of treatment. In cases where an allergic component is in the foreground of the clinical picture specific desensitization is advised, but positive effects are obtained particularly in early cases; with chronicity the nervous aspect becomes predominant.

The main aim of our work was the elaboration of a method of suppressing the pathological dominant over a long period, and thereby facilitating its gradual extinction. As an unconditioned agent which is known to suppress bronchial spasm directly, adrenaline was used. Where contra-indicated, as in hypertension or hyperthyroidism it was replaced by syntophilin, or ephetonin. From the experimental results mentioned above it is clear that when adrenaline is given alone, especially in large, single doses, it cannot produce a lasting effect, a fact well recognized clinically. In order to produce a less drastic but at the same time more protracted effect we gave adrenaline in minimal doses, in combination with indifferent conditioned stimuli. In this way we intentionally effected the "penetration" of its action into the cortical level and created what could perhaps be called a kind of a new "competitive" sympathicotonic dominant.

The procedure was as follows: The individual optimal dose is first determined. Using the adrenaline or ephetonin test, a dose is found which increases the vital capacity by 200–300 cc without causing significant changes in the cardiovascular apparatus. An initial dose of 0·1 cc of adrenaline is used; the dosage is increased as necessary. It is seldom necessary to use a dose larger than 0·3 cc for longterm treatment. It can usually be lowered later in the course of treatment.

Since the basic aim is to suppress the pathological excitability for as long as possible, in more serious cases treatment is started as in cases of status asthmaticus. In the first few days—according to the patient's condition—injections of adrenaline are given every 3, 4, 6, 8 hr (in a minimal dose, which has been previously determined). After several days it is usually sufficient to give an injection twice daily, then once a day gradually prolonging the intervals between injections.

In the first few days adrenaline is given alone; after approximately 10–20 injections it is generally possible to use a conditioned stimulus. The strongest stimulus is the injection procedure, so that any indifferent sterile solution injected subcutaneously can be used. In fact a mixture of sterile physiological saline with small doses of brom-caffein ("*solutio antiasthmatica*") is used. As a weaker conditioning factor we use an olfactory stimulus (a weak menthol solution for example). After each injection the patient is left at rest for half an hour inhaling the menthol solution from a piece of gauze. The effects of the conditioned stimulus are evident during an attack, and when dyspnoea occurs. But even during an intermission, it is generally possible to demonstrate the release of latent spasm spirometrically or by other objective methods (Fig. 1). CHVAPIL (1952) also demonstrated a conditioned decrease of eosinophils in our patients.

Depending on the intensity of the conditioned association and the general state

VOL.
5
1960/6

of the patient the injection of adrenaline is gradually more frequently alternated with the injection of the indifferent solution, or the inhalation of the menthol solution alone.

After the disappearance of the symptoms, which usually occurs within 6 weeks at the latest from beginning hospital treatment, the patients are discharged for outpatient treatment. For a period of about 6 months the injections are given at the outpatient department, first twice weekly, then once a week, and later less often. We advise the patients to inhale at home at last once a day with menthol solution on days

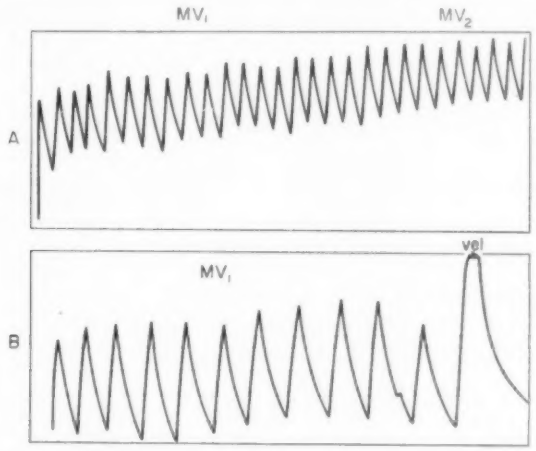

FIG. 1.—(a) Spirogram before injection of the conditioned stimulus (1 cc "*solutio antiasthmatica*") (b) Spirogram 10 min after the injection.

when they do not get the injections; with the help of this inhalation they sometimes succeed in suppressing a slight attack of asthma. For patients who mostly suffer from nocturnal attacks of asthma we prescribe salicylate and ephetonin powder, to be taken daily before going to sleep. In this way it is possible to considerably reduce the dosage of anti-asthmatics, which had previously often been taken in large doses.

The scheme is the rough outline for cases where hospitalization is indispensable. In slighter cases it is possible to proceed earlier with outpatient treatment after a preliminary examination and preparatory treatment at home. In children it would be adequate to substitute injections by inhalations of anti-asthmatics and combine it with an indifferent inhalation factor.

With regard to the general tonization of the CNS, it is necessary to proceed very individually, depending on the predominance of the state of heightened excitability, inhibition or total exhaustion. In exhaustive states good results were obtained with a solution of bromide and caffeine, huge doses of vitamin C and sometimes sexual hormones (as we are concerned with the non-specific effect on the total metabolism we recommend androgenous hormones for both women and men). In more severe cases with a prevalent inclination to supermarginal inhibition we used sleep therapy, mostly combined with insulin sub-shock. Sleep therapy must be used with great caution on account of the lowered expectoration, and the predominance of parasympathetic tone even during the physiologic sleep. It was, therefore, carried out either in repeated short-term courses (2–3 days) or for a fortnight in the form of

a prolonged sleep at night. Insulin is given in the morning in doses producing hypoglycaemia without a state of unconsciousness. The deep, physiological sleep which occurs after the interruption of the hypoglycaemia is prolonged in suitable surroundings by minimal doses of drugs. This method of sleep therapy, alternating with stimulation of the CNS is described in detail elsewhere (MICHALOVÁ 1956).

RESULTS

102 patients have been treated, some of whom have been under observation since 1952. Nearly all the cases had suffered from bronchial asthma for at last 5 years; usually the patients were admitted in an exacerbation of the illness. Almost all of them had previously received different types of therapy. 43 patients improved, 14 of whom made practically a lasting recovery and 29 showing an essential qualitative change for the better. In 26 cases the treatment was discontinued; in the remaining 33 cases an exact evaluation was impossible. These were patients who lapsed after a short period of improvement. The following are some illustrative cases:

In 1951 the 17 year old patient J. A. K. came under our care. He had suffered from bronchial asthma for 10 years and had severe daily attacks for many months on end specially during the summer. On admission to hospital he was seriously ill—asthenic, dyspnoeic and generally restless (pulse constantly 120–140), evidently as a consequence of the continued use of excessive doses of drugs. No definite signs of allergy were found in the humoral sphere (blood K, Ca, eosinophils). Sleep therapy led to a general tranquilization and after undergoing clinical and outpatient treatment according to the above scheme, the patient recovered completely. He successfully matriculated, and has already been working successfully for several years. The vital capacity as rest is approximately 5,000 cc and changes in respiratory function cannot be demonstrated even by objective methods. Sometimes dyspnoea occurs as a result of a severe cold, and once after excessive physical strain. It could always be quickly suppressed.

The patient J. has also suffered from bronchial asthma since childhood. His first attacks occurred at the age of 5, following pneumonia, from then on he suffered every winter from severe asthmatoid bronchitis and frequent attacks of bronchial asthma. He was treated by autovaccines, diet and climatically, all without lasting effect. He came to us at the age of 10. After hospitalization at the childrens' hospital he was treated as an outpatient according to our scheme. He still has a tendency to get bronchitis and has had pneumonia three times during the last 5 years, but the disposition for asthma has been lowered radically and hardly any attacks have occurred during recent years. The boy feels practically well.

The patient A. had suffered from bronchial asthma from 1948. From 1951 onwards he had dyspnoea and attacks daily. He stated that for a period of 4 years not a single day had passed without his being obliged to take strong anti-asthmatic drugs. We have been treating him since 1955. For a period of weeks to months he requires no medication, a slight dyspnoea only appears after intercurrent infections or bronchitis, and this can now be controlled by syntophilin.

The course of the illness of the patient E. P. is worth recording, since she suffered from a typical allergic vasomotor rhinitis which appeared regularly at the beginning of summer and lasted about 2 months. At the insistence of the patient she was treated with sleep therapy combined with insulin and followed by small doses of adrenaline according to the above scheme. In the summer following the course of treatment, the patient was symptom-free. In the following years she only came for injection treatment a month before the expected "onset" of symptoms. But since that time there is an essential change in the course of the illness; the vasomotor rhinitis is milder and conjunctivitis, which troubled the patient most, has disappeared completely.

Many of our patients are over the age of 40. A long-continued illness has evoked chronic bronchitis, emphysema and often cardiac difficulties in most of the cases so that it is impossible to reach a state of complete health. But we succeeded in suppressing or in lowering the spastic disposition to a considerable degree, so that it is possible to speak of a sort of "desensitization" in the real sense of the word as it refers to

VOL.
5
1960/6

nervous regulatory mechanisms. The irritant stimuli lose their effect since they impinge upon less excited centres.

DISCUSSION

In spite of the ample experimental material there is undoubtedly much that is hypothetical in these considerations and it will be necessary to follow these complicated relationships both experimentally and clinically for a long period. Theoretically it is possible that the positive effect is produced by long continued, adequate dosage, i.e. by both the injection of small doses of exogenous adrenaline and by the mobilization of its endogenous effect through the medium of conditioned stimuli. The question of individual and rational dosage has undoubtedly a basic significance in experimental therapy, and ever since the time of the old "Arndte-Schultze law" of the different action of large and small doses, the necessity for differentiated dosage has been increasingly emphasized. Much light has been thrown on this by the work of WEDENSKY (1904) and UKHTOMSKY (1926) on parabiosis, i.e. on the two-phase of pharmacodynamic and tonic substances. Another question which must be dealt with is the extent of the psychotherapeutic influences. A good doctor-patient relationship, and confidence in the treatment are without any doubt of assistance to the process of treatment. This is, however, only a question of a nonspecific general psychic tonicization which cannot interfere in a decisive measure with the autonomic pathogenetic chain. One of the proofs that mechanisms are involved which have their basis mainly outside second-signal, i.e. pure psychic, influences is the reproducibility of analogous mechanisms in animal experiments. NOELPP and NOELPP-ESCHENHAGEN (1951) for example, evoked asthmatic attacks in guinea-pigs by means of histamine and conditioned sound stimuli. MAKARYCHEV and KURTSIN (1951) succeeded in producing a prolonged and stable change in blood pressure in dogs by the continued injection of adrenaline and conditioned stimuli (physiological saline and a sound stimulus).

SUMMARY

In the introduction the origin of bronchial asthma is discussed and reference made to three main links of the pathogenetic chain:

(1) The inflow of excitory impulses from the periphery (by way of interoceptors or chemo-receptors).

(2) The development of the pathological dominant in the region of the vagal centres.

(3) The weakening of the higher regulatory mechanisms in the cerebral cortex.

A comprehensive form of therapy is described. After preliminary antibiotic and antiphlogistic treatment special attention is devoted to the suppression of the pathological dominant, by means of long term conditioning with small doses of adrenaline. The whole tonicization of the CNS is achieved by sedative therapy, vitamins and hormones, and in some cases by sleep therapy in combination with insulin.

Experiences with morethan 100 patients are described.

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VOL.
5
1960/6

Journal Psychosomatic Research, 1961, Vol. 5, pp. 139 to 144. Pergamon Press Ltd. Printed in Northern Ireland

REPORT OF MEETING

1er Congrès de Médecine Psychosomatique—Vittel 8-9-10 Juli 1960

1er Congrès de Médecine Psychosomatique de langue Française was held at Vittel on 8, 9 and 10 July 1960, under the Presidency of Prof. JEAN DELAY

Approximately 300 French-speaking representatives of 17 nations attended the following programme:

Friday 8 *July* 1960

Professeur JEAN DELAY

Perspectives psychosomatiques (Exposé du Président)

1er Theme: Aspects théoriques et pratiques de la Médecine Psychosomatique.

Présidence: M. le Professeur J. DE AJURIAGUERRA (Genève).

Présentation par le Président.

RAPPORT:

Résultats de l'enquête sur la Médecine Psychosomatique.
CH. BRISSET et M. SAPIR (Paris).

COMMUNICATIONS:

NACHT S. et HELD R. (Paris).
Maladies psychosomatiques ou malades psychosomatiques.

STOKVIS B. et HOBERGER I. A. D. (Leyden).
Considérations critiques sur la théorie et la pratique de la recherche psychosomatique.

PERRIER F., LECLAIRE S. et ROSOLATO G. (Paris).
Déterminisme au sens du symptôme psychosomatique.

CHARANKOV E. (Sofia).
Le Psychique dans la causalité, le mécanisme intime et la psychothérapie.

TZANCK R. (Paris).
Prétention pathogénique et médecine psychosomatique.

MICHAUX L. et DUGAS M. (Paris).
Les interactions organiques affectives de l'anorexie mentale.

WEILL J. et LANDRY M. (Paris).
Principes de la médecine psychosomatique chez l'enfant.

LAMBERGEON S. (Mlle) (Paris).
Transfert et contre-transfert en médecine psychosomatique.

Saturday 9 *July* 1960

Médicine psychosomatique

Aspects théoriques

COMMUNICATIONS:

ALBERT A. (Paris).
Quelques réflexions sur les troubles psychosomatiques et leur traitement.

MORIN G. (Villefranche-sur-Mer).
Les fondements psychosomatiques d'une nouvelle typologie.

VOLGYESI F. (Budapest).
Les aspects psychoanalytiques, psychosomatiques et actifs complexes des problèmes de la psychothérapie moderne.

PARIENTE M. (Hôpital psych. du Loiret).
De la pathologie fonctionnelle à la médecine psychosomatique.

ENKE et ROTAS (Fribourg-en-Brisgau).
Les méthodes cliniques actives dans le cadre de la psychothérapie des malades internes en traitement dans une clinique.

KURTH W. (Wiesbaden).
De la signification et de la valeur de la psychothérapie en médecine psychosomatique.

GUENSBERGER E. (Bratislava).
Quelques remarques sur les mécanismes fondamentaux spécialement sur ceux de la différence entre le rôle du facteur psychologique comme fait anamnéstique et comme mécanisme pathogénique.

LORAS O. (Lyon).
La personnalité des asthmatiques. Perspectives phénoménologiques et psychothérapiques (observations de cures).

RAIMBAULT E. (Paris).
Psychothérapie de groupe en psychosomatique; bilan d'une expérience de recherche et de traitement avec un groupe de malades aouffrant d'asthme bronchique.

Médecine psychosomatique

Applications

JANOTA O. (Prague).
Considérations sur les troubles psychosomatiques dans la dépression endogène.

BARAHONA FERNANDES H. (Lisbonne).
Thérapeutiques pharmaco-psychologiques.

CATTALANO-NOBILI et CERQUETELLI (Rome).
Traitement pharmaco-psychique de l'anxiété dans certaines névroses à localisations différentes.

FUCHS M. (Mlle.) (Bâle)
Le traitement de certaines manifestations somatiques au cours des états dépressifs.

VOL.
5
1960/6

BÉCACHE J. (Paris).
Médecine psychosomatique et technique électronique.
PAILLARD-VARIN M. (Mme) (Vittel)
Rôle psychosomatique des facteurs climatiques.
GEBER M. (Mlle) (Paris)
Troubles digestifs psychosomatiques de l'enfant.
WEILL J. et BERNFELD S. (Mme) (Paris).
Les syndromes endocriniens d'origine psychique.
WEILL J. et SAUTIER C. (Mme) (Paris).
Dépistage psychosomatique en clinique pédiatrique.
MICHEL-WOLFROMM H. (Mme) (Paris).
Abords psychologiques de l'aménorrhée.
HARTEMANN J. (Nancy).
Les vomissements de la grossesse rentrent-ils dans le cadre de la médecine psychosomatique?
LAMBLING A. et BURGER J. (Paris).
Formes cliniques psychosomatiques de la maladie ulcéreuse.
VILLA J. L. (Lausanne).
Les troubles digestifs fonctionnels chez l'émigré italien en Suisse Romande.
BEGOIN J. (Plateau d'Assy, Haute-Savoie).
Aspects psychosomatiques du traitement des tuberculeux pulmonaires en sanatorium.
CHIPKOVENSKY N. (Sofia).
Rôle du surmenage dans l'hypertension des étudiants.
BERGOUIGNAN M. et DEMANGEAT A. (Bordeaux).
Les lombalgies, perspectives psychosomatiques.

OL.
5
0/61

Relaxation

Sous-section obstétricale

Présidence: M. le Professeur H. DE WATTEVILLE (Genève).

CHERTOK L. et MONDZAIN M. L. (Mlle) (Paris).
Introduction à l'etude de la relaxation en obstétrique.
GEISENDORF W. et KOCHER PH. (Genève).
La part de la relaxation dans la méthode psychoprophylactique de la préparation à l'accouchement.
LUKAS K. H. (Tübingen).
Tension et détente.
MAYER M. et MORALI-DANINOS A. (Paris).
Aspects psychosomatiques de la relation mère-enfant.
NOTTER A. (Lyon).
Intérêt psychique et psychologique de la relaxation durant la gestation et l'accouchement.
PRILL H. P. (Würzbourg).
Le problème d'une relaxation psychosomatique en obstétrique.

2e Théme: La Relaxation

Présidence: Professeur J. H. SCHULTZ, Berlin.

Présentation par le Président:

Somatisation et psychothérapie.

RAPPORTS:

DE AJURIAGUERRA J. (Genève) et CAHEN M. (Mlle) (Paris).
Tonus corporel et relation avec autrui. L'expérience tonique au cours de la relaxation.

KAMMERER TH. et DURAND DE BOUSINGEN R. (Strasbourg).
Relaxation et psychothérapie.

FRIEDMANN A. (Biel-Bienne).
Training autogène. Quelques remarques sur la place de cette technique dans le traitement des troubles fonctionnels dits psychosomatiques et dans la psychothérapie abyssale.

STOKVIS B. (Leyden).
Possibilités et limites de relaxation dans la médecine psychosomatique.

SAPIR M., REVERCHON F., PHILIBERT R. et JAVAL. I. (Mme) (Paris).
Valeur et signification du training autogène.

BINSWANGER H. (Zürich).
Applications du training autogène à des affections psychosomatiques.

Sunday 10 *July* 1960

Théorie de la Relaxation

COMMUNICATIONS:

VAN DER HORST L. (Amsterdam).
Traitement par la détente en neuro-psychiatrie.

LOWYS P. (Sanatorium "Roc des Fiz", Haute-Savoie).
Réflexions d'un médecin non psychiatre sur la relaxation.

KRAPF E. E. (Genève).
Relaxation psychosomatique et tranquillisation médicamenteuse.

KLEINSORGE H. (Iéna).
Le training organique dirigé.

JUS A. (Varsovie).
Etude polygraphique de la relaxation.

MEIER O. (Brittnau).
Conduite du médecin vis-à-vis des difficultés se déclarant pendant les premières semaines du training autogène.

NEUSS K. (Bad Rehbourg).
Théorie et pratique du training autogène.

EHRHARDT H. (Hambourg).
La relaxation, la potentialisation réciproque des méthodes psychosomatiques.

KLUMBIES G. (Iéna).
Traitement par la relaxation hypnotique (avec projection d'un film).

LANGEN D. (Tübingen).
La différence entre l'hypnose fractionnée et l'hypnose active graduée.

VOL. 5 1960/6

Applications de la Relaxation

BENOIT J. C. (Paris).
Training-autogène et "liquidation morale" des réminiscences traumatiques et des phobies.

JARREAU R. et KLOTZ R. (Mme) (Paris).
Les paratonies cruciales en relaxation.

JACOBSON E. (Chicago).
Les principes soulignant les méthodes de la relaxation scientifique.

LEEUWE J. DE (La Haye)
Relaxation et activité optimale.

BEGOIN J. et BEGOIN A. (Plateau d'Assy, Haute-Savoie)
Relaxation de groupe en cure sanatoriale.

BETLHEIM S. (Zagreb).
Contribution à la relaxation d'apres Schultz concernant les troubles subjectifs à propos de l'hypertonie essentielle.

SIVADON P. (Bruxelles).
Relaxation dans les névroses du travail.

WIESENHUTTER E. (Wurzbourg).
La relaxation et la réadaptation.

OL.
5
0/61

Médecine Psychosomatique.

Aspects théoriques et pratiques.

VALABREGA J. P. (Paris).
Orientation pratique et théorique de la recherche psychosomatique.

MICHALOVA C. (Mme) (Prague).
Contribution à quelques problèmes d'étiologie et de pathogénie du point de vue du nervisme.

DICK P. et GARONNE C. (Genève).
Essai de traitement des états de tension par un tranquillisant de structure chimique nouvelle.

SARRO R. (Barcelone).
Le point de vue psychosomatique dans le système médico-anthropologique de José de Letamendi (1827–1897).

UNGHER J. E. CIUREA et VOLANSKI D. (Institut. I. P. Pavlov., Bucarest).
Troubles de l'activité nerveuse supérieure et les manifestations végétatives dans les états névrotiques provoqués expérimentalement chez le chien.

SOLOMONIVICI A. (Institut I. P. Pavlov, Bucarest)
Le rôle du facteur somatique dans l'apparition et l'évolution de la névrose asthénique.

COPELMAN L. (Bucarest).
Les bases neuro-endocriniennes de la médecine psychosomatique.

Théorie de la Relaxation

COMMUNICATIONS:

CAHN R. (Paris).
Transfert et contre-transfert dans le training autogène.

THIS B. (Paris).
Relaxation et image du corps.
HELD R. et REVERCHON F. (Paris).
Psychanalyse et relaxation.
RECHENBERGER H. G. (Rheydt-Giesenkirchen).
Expérience du drame symbolique.
SALFIELD (Derby).
Existence et training autogène.
STUCHLIK J. (Prague).
La relaxation, son essence, ses formes.

Applications de la Relaxation

SEARRA-DINIS J. (Lisbonne).
Expérience clinique de six ans au sujet de la relaxation.
HATTINGBERG J. V. (Bad Rothenfelde).
Le traitement de l'insomnie chronique chez les ouvriers par le training autogène.
KLOTZ H. P. (Paris).
Intérêt de la relaxation dans la spasmophilie.
ALBERTS M. (Rehau).
Le training autogène chez les enfants et les adolescents.
BINDER H. (Hambourg).
Le training autogène chez les traumatisés du crâne.

Summaries of these contributions have already been published as a supplement to the *Revue de Médecine Psychosomatique*, Vol. **2.** No. 2., 1960.

VOL.
5
1960/6

Journal of Psychosomatic Research, 1961, Vol. 5, pp. 145 to 146. Pergamon Press Ltd. Printed in Northern Ireland

NOTICES

THE SOCIETY FOR PSYCHOSOMATIC RESEARCH

Programme for 1960–1

October 6
Dr. ARNOLD LEVENE
Cancer, a psychosomatic disease?

November 11–13
CONFERENCE *at the Royal College of Physicians*
Psychosomatic disorders in adolescents and young adults

December 1
Mr. J. C. SCOTT
Organic effects of "stress" in the disc syndrome

January 26
Dr. LINFORD REES
Psychiatric illness associated with female reproductive function

February 16
Dr. A. LASK
Aspects of personality traits in asthma
Discussion to be opened by Dr. Michael Balint

March 23
Discussion on Syndrome Shift

April 27
Mr. PAUL SENFT
Psychoanalysis and Existential Analysis, a comparative study in one case

May 12–14
Conference at the *Royal College of Physicians*
Adult life: The role of psychosomatic disorder
Annual General Meeting

Meetings are held at 8.15 p.m. in the Marcus Beck Library of the Royal Society of Medicine and are preceded by dinner at 7 p.m. for 7.15 p.m.

Additional Meetings may be arranged by Council, and these will be notified to members

FORTHCOMING CONFERENCE

The **French Gastro-Enterological Society** and the **French Society for Psychosomatic Medicine** will hold a meeting on 8th and 9th July 1961 on the Psychosomatic Approach in Gastro-enterology. The principal theme will be Gastro-Duodenal Ulceration. Professor P. B. SCHNEIDER will preside and the meeting will be held in Lausanne. Please send titles of papers and a summary to:—

Dr. L. CHERTOK,
Société française de Médecine psychosomatique,
54 Avenue de la République,
Villejuif (Seine), France.

The **Second International Conference on the Psychosomatic Aspects of Malignant Disease** will be held in Paris on August 27, 28, 29 of 1961. Those interested in presenting papers or in attending should notify:

Dr. L. LESHAN
144 East 90 Street
New York 28, N.Y.
U.S.A.

VOL
5
1960/

Journal of Psychosomatic Research, 1961 Vol. 5, pp. 147 to 154. Pergamon Press Ltd. Printed in Northern Ireland

BOOK REVIEWS

DORIS ODLUM: **The Mind of Your Child.** W. and G. Foyle Ltd., London, 1960, 108 pp., 4s.

THIS is a concise and clearly written book of advice for parents on the emotional development of the child from babyhood to pre-adolescence. After a rather slow start, it offers sound and up-to-date advice on the common problems that parents may meet in their child, including that of the eleven plus examination. It seems to be designed for those of a reasonable standard of education and it may well help them to avoid a number of mistakes in upbringing. How far any such book can help the over-anxious parent is a question that is not easy to answer; it certainly cannot take the place—in real trouble—of personal support and help by someone skilled in these matters.

W. WARREN

Neuro-Psychopharmacology. Proceedings of the First International Congress of Neuro-Psychopharmacology, Rome, 1958. Edited by P. B. BRADLEY, P. DENIKER and C. RADOUCO-THOMAS. Elsevier Publishing Co. Amsterdam, London, New York, Princeton, 727 pp., £6. 15. 0.

IT IS hard to justify the purchase of this beautifully produced and in every way handsome volume, for the price is high, and the material already somewhat out-of-date. Have we not arrived at the stage when medical publishing houses should not take on the printing of symposia such as this? The proper place for research publications is the research journal. What so often happens is that there is only a re-hashing of old material, a synopsis of an author's previous work, and a good deal of verbal interchange between the different participants. The editors have done an excellent job here with their material, and many of the major irritations of the printed symposium are avoided. But was it really necessary? For those who are interested the volume contains the proceedings of the First International Congress of Neuro-Psychopharmacology—a Congress attended by more than 500 delegates. The Congress discussed the following subjects:—The Methods and Analysis of Drug-induced Behaviour in Animals, and of Abnormal Mental States in Man. Comparisons were made between men and animals under the influence of psychotropic drugs, and there were special sessions on the endogenous psychoses, the effects of the psychotropic drugs on the Psychiatric Services and so on. 133 short papers are also printed reporting original observations in this field, ranging from drug action and endocrine behaviour, to the effect of tranquillizers on the midbrain. At the time of publication these papers are sixteen months out-of-date—a period which speaks for itself. Some diminution in the spate of medical publications must occur. I suggest that a start could be made in this field of the publication of symposia.

DENIS LEIGH

ERWIN H. ACKERKNECHT: **A Short History of Psychiatry.** Translated by S. Wolff. Hafner Publishing Co., New York, London, 98 pp., 25s.

THIS is an excellent precis of the historical development of psychiatry, an enormous amount of information being compressed into its 98 pages. Its purpose is presumably to stimulate interest in this field, for of necessity much of the information given has otherwise little meaning. For instance, lists of writers who contributed during a certain period mean nothing unless they are to be used as a guide for further reference. Perhaps there is just a little too much detail, and the book would have

made more interesting reading if the minor names had been omitted. English psychiatry gets little mention; and, as is the danger in such books, a misleading impression may be given by the brevity of the text. For instance, Bethlem Hospital has two references, one to opening as a hospital in 1377, and the other in a note on John Haslam—"Haslam (1798, he was apothecary to the famous and notorious Bedlam Hospital in London till he was dismissed in 1816)". Bethlem may have been both famous and notorious, and Haslem was indeed dismissed, but the statement does justice to neither. What is needed, rather than precis history, is a series of monographs dealing with the historical development of certain concepts, or with biographical studies. But if this little book serves to stimulate interest in the subject it may have contributed something toward this goal.

DENIS LEIGH

GRANTLY DICK-READ: **Childbirth without Fear.** Fourth Edition revised and enlarged. Wm. Heinemann Medical Books Ltd., London, 1960, XV, +266 pp., 12s. 6d.

GRANTLY DICK-READ was made of the stuff of pioneers, fixed in his purpose, with a burning faith in the truth of his message, and with an emotional, even mystical, approach to his subject. All his books are worth the reading, and this edition of *Childbirth without Fear*, completed just before his death, is compelling in the intensity of feeling with which it is written. Interspersed with homilies, and autobiographical details which, although sentimental, are never mawkishly so, is the matrix of his method, his own observations and thoughts on all to do with the processes of childbirth. No doctor in practice could fail to benefit from reading this book; it is a wonderful example of how the psychosomatic approach to medicine can illuminate a problem. DICK-READ's works will become the classics of the future—for readers of this journal they are of unique interest.

DENIS LEIGH

THEODORE LIDZ: **Zur Familienumwelt des Schizophrenen.** (Sonderheft der "Psyche") Ernst Klet Verlag, Stuttgart, 153 pp., DM 8.

IN their double edition for August/September 1959, the publishers of *Psyche* present a collection of papers by a team of American psychiatrists and psychiatric social workers, headed by Prof. THEODORE LIDZ, on their research into the families of schizophrenic patients. The papers are based on an intensive study of 16 young schizophrenics between the ages of 15 and 30 who were in-patients in the Yale Psychiatric Institute, and their families. With the exception of an introduction by Prof. LIDZ, they had all been previously published during 1957/59, and have been translated by Dr. HORST VOGEL and Dr. PETER KRAUSSER.

Whilst accepting the possible importance of genetic factors in the causation of schizophrenia, Prof. LIDZ and his team were impressed by the occurrence of severe disturbances in the families of their patients, either in the form of marked abnormality in one or both parents or, often concomitantly, the existence of grossly abnormal interpersonal relationships within the families. The team is psychoanalytically orientated and their research is based on the concept that environmental influences may play an important part in schizophrenic illness. They see it as a manifestation of failures in personality development, a retreat from interpersonal relationships and from reality. By an exhaustive investigation of the family environment in which their patients grew up, they throw light on the circumstances in which these failures occurred. The personalities and roles within the family of either parent, and marital as well as parent-child relationships are described, revealing many abnormal features. The bearing of these on the personality development of the patients is discussed in the light amongst other things of difficulties caused in psycho-sexual development by lack of adequate parent figures with whom the patient can identify, by faulty and often mutually de-valuing and destructive relationships between the parents, and between them and the child who became a patient. The authors stress the importance of maintaining contact with the families of their patients not only in order to gain a

better understanding of the patient, but to help the parents with their problems relating to their child's illness, and thus prevent them from undermining the treatment or withdrawing the patient prematurely from the clinic.

The findings are not validated against a control group or compared with those of other studies made in this field, nor are claims made for their general validity for all schizophrenic patients. It is strongly suggested, however, that this form of approach and study may be of great value in the understanding and treatment of schizophrenic illness.

To the German reader, these papers may be of special interest as they present a viewpoint less frequently met with in German psychiatry and in many ways alien to the German concept of psychotic illness and its treatment. By arranging for their translation into German and publication in their journal, the editors of *Psyche* have made available to their readers reports on some valuable and thought-provoking research work done at the Psychiatric Institute of Yale University.

I. Lissman

The Registrar General's Statistical Review of England and Wales for the Three Years 1954–1956, Supplement on Mental Health. H.M.S.O., 1960, 198 pp., 11s. 6d.

The Supplement is a further continuation of the series which began in 1949 on Mental Health Statistics. It provides detailed statistical tables of admissions to and discharges from mental and mental deficiency hospitals for the three years 1954–56.

The first part consists of summary tables with adequate commentaries, showing the trends in the hospital populations analysed with respect to age, sex, status, diagnostic groups, social class and areas of residence.

The second part gives more detailed statistical tables of raw data relating to the summary table. An interesting special table gives details of admissions, discharges and deaths for each mental hospital for 1955.

In spite of the rise in admission and discharge rates the resident population of the hospitals decreased. Second and subsequent admissions rose by 79 per cent for women between 1951 and 1956; the corresponding figure for men was 75 per cent. The overall statistics demonstrate that the once "closed door" of the mental hospital has now become the "revolving door". It is amongst the over 75 age group that a differential climb in the hospital population has occurred.

This detailed information underlines the changing pattern of the mental hospital population.

J. Johnson

F. V. Smith: **Explanation of Human Behaviour.** 2nd Edition. Constable & Co. Ltd., London, 1960, 460 pp., 30s.

This is a revised and enlarged edition of Professor Smith's book of the same title published in 1951. The organization is very similar to that adopted in the first edition: A theoretical–methodological introduction well-illustrated by examples from psychology and other sciences; a section dealing with the theories of McDougall, Allport, Lewin and the Gestalt and Freudian approaches; and finally a section dealing with Behaviourist systems.

The expressed aim of this volume has been to present "a number of related issues which are associated with the explanation of human behaviour" and to give some account of the historical context in which they have arisen. This aim has been amply realised and the book must therefore have a wide appeal.

It may appear that the ground covered is identical with that covered by other texts (e.g. Woodworth's *Contemporary Schools of Psychology*) yet it has certain salient advantages over the available alternatives; it is lucidly written, very readable, and has a useful bibliography with a number of references to recent publications. Any immediate impression that the material is "dated" is dispelled

by the presentation of theoretical issues as very much alive and the concern of psychologists today, and also by the introduction of relevant contemporary material.

The book will be of undoubted value as an introductory text for undergraduate students of psychology, and as preliminary reading in psychology for psychiatrists, social workers, and the like.

H. R. BEECH

Les Applications de la Medicine Psychosomatique. Edited by P. ABOULKER, L. CHERTOK and M. SAPIR. Expansion Scientifique Francaise, 1960, pp, 138, 10.50 N.F.

THIS is a series of brief articles on a variety of topics dealing with the psychosomatic approach to medicine. MONTASSUT and CHERTOK put the case in favour of this approach, and describe the organisation of the psychosomatic department at Villejuif. SAPIR and HELD deal in separate articles with the sociological aspects of psychosomatic medicine, and there are more specific contributions by LAMBERGEON and MICHEL-WOLFROMM on skin disorders and gynaecological disturbances. Other subjects include industrial medicine and life in sanatoria. The book will be of interest to general practitioners and those to whom the psychosomatic approach is relatively unfamiliar.

DENIS LEIGH

Advances in Psychosomatic Medicine. (Symposium of the Fourth European Conference on Psychosomatic Research, Hamburg. 1959.) Edited by A. JORES and H. FREYBERGER, S. KARGER, Bale and New York, 1960, p. 328, 58 Swiss francs.

THIS is the first of a series of monographs which are to appear from time to time dealing with the problems of psychosomatic medicine. It consists of the papers given at a meeting of research workers in this field held in Hamburg in 1959. Ably edited by Professor JORES and Dr. FREYBERGER and beautifully produced, it reveals something of the present position of the subject in Europe. A start has been made and a promising one, but a great deal of work is necessary on all fronts before we can be satisfied. The interest of this book to our colleagues in the U.S.A. and Canada will be more historical than scientific—we are going through a phase which they have already experienced and the book should be taken in this light.

DENIS LEIGH

ROBERT REIFF and MARTIN SCHEERER: **Memory and Hypnotic Age Regression.** International Universities Press, 1959, pp. 253, $5·00.

THE concept of age regression in hypnosis has always attracted a good deal of interest, and there has been much dispute about the possibility of faking results. There is very little doubt nowadays among experts that hypnotic age regression is a genuine phenomenon and that if proper precautions are taken, it cannot be faked. The book under review, which is essentially a Ph.D. thesis, done by one of the two authors under the guidance of the other, does not add very much to this conclusion; indeed, one would normally have expected an experiment of this type to be reported in very much briefer outline as a Journal article. In essence the experiment consisted in having a group of hypnotized subjects undergo age regression to various ages, and to compare their performance with that of the control group of non-hypnotized subjects who were trying to fake regression to the same ages. Marked differences were encountered, and the results are presented in a very convincing fashion by the authors. They also tried to link up their findings with a rather woolly theory of memory which, while it serves to pad out their experimental material, does not seem to add very much to their own findings.

H. J. EYSENCK

VOL.
5
1960/6

ANTHONY STORR: **The Integrity of the Personality.** Heinemann, 1960, pp. 174, 15s.

A POPULAR book on a medical subject is usually supposed to be of value only to the layman. In psychiatry, however, such is the manifold complexity of the subjects related to it, a popular book is required in order that the bio-chemist (to take an extreme case!) can acquaint himself with the business of the psychotherapist.

Dr. STORR's book, therefore, is of treble value. It is in the ordinary sense a good popular book, firstly, because of the clear and non-technical language in which it is written, secondly, because it concentrates on the basic mechanisms of the doctor/patient relationship and, thirdly, because it avoids those more technical and controversial topics which so often alienate the enquiring layman. As a description of the method of treatment it could hardly be better.

One recalls, however, that what started as a method of treatment grew into a theory of mental disorder, and psychiatry, unfortunately, has not yet reached the stage and probably never will in which one theory can account for the causes of all mental disorders, psychoses and psychoneuroses alike. To say that "schizophrenia is . . . . . a human reaction and not a disease" (p. 56) may serve to explain the content of some of the symptoms in an individual case, but it is never likely to lead to the formulation of a theory explaining why the disease occurs in the first instance.

J. P. DEWSBERY

W. J. F. VAN DER BIJL: **Studies on the Technique of Skin Testing in Allergy.** H. E. Stenfert Kroese, N. V. Leiden, 1960, pp. viii + 100, 12·50 Dutch guilders.

OL.
5
0/61

THIS book has been written to supply medical practitioners interested in allergy with technical information about skin testing. The value of skin testing in establishing a diagnosis has not been considered. Unfortunately a critical review of various aspects of skin testing has not been included. The personal studies of the author, although informative, will only have limited interest.

A. W. FRANKLAND

WILDER PENFIELD and LAMAR ROBERTS: **Speech and Brain Mechanisms.** Princeton University Press London: Oxford University Press, 1959, pp. 286, 35s.

WILDER PENFIELD's stimulation experiments on the cerebral cortex of conscious patients have substantially added to the knowledge of the higher brain functions. In this work, the authors are concerned with the effects of cortical excisions and of electrical stimulation on speech. They frequently observed transient aphasia after operation on the minor hemisphere. They developed a method of "mapping the speech cortex" by using electrical interference during operation for excision of epileptogenic foci. The "aphasia of electrical interference" did not show the same variety of patterns as that produced by brain lesions. This kind of disturbance produced "negative" symptoms only. The areas mapped out with this method were found to be considerably bigger than the traditional aphasia regions of the cortex, but the latter were parts of them. The functional integration of these areas is believed to depend upon their connection with the thalamus.

In their theoretical discussion the authors distinguish between experimental and conceptual records in the brain. There are "ganglionic equivalents" of words and of concepts which are preserved somehow in the "centrencephalic" system which includes the thalamus. This theory of the speech mechanisms is reminiscent of that of the early localizers of the speech functions. This is not surprising. PENFIELD's work and that of other clinical experimentalists has inevitably led to a revival of localizing tendencies couched in modern terminology.

The final chapter is concerned with the learning of languages. This is a problem very close to the senior author's heart although it does not arise directly from the main clinical observations reported in the preceding chapters. The authors rightly complain that the teachers of languages do not consider

the biological time-table in choosing the age for learning new languages. The optimum age is 4–10 years. Living in a bilingual country, the authors have first hand experience with this problem. It is to be hoped that educators will take note of such well-informed advice the soundness of which is born out by common experience.

E. STENGEL

R. W. PARNELL: **Behaviour and Physique, An Introduction to Practical and Applied Somatometry.** Edward Arnold, London, 1958, pp. 134, 28s.

PHYSICIANS have been interested in studying relationships between physical type and susceptibility to diseases since the time of Hippocrates. The humoral theories of ancient Graeco-Roman medicine were greatly elaborated by Galen who described characteristic temperamental traits for various physical types and constituted not only a doctrine of disease causation but also attempted to account for individual differences in mental and physical attributes and disease susceptibility.

The modern study of constitution started with the work of Beneke and Di Giovanni, later receiving a great impetus by the publication of Kretschmer's book *Physique und Charakter*. In recent years the two main approaches to the assessment of body build have been Factorial analysis and Sheldon's method of somatotyping. Sheldon described three components of physique which are alleged to be derived from the three primary ectodermal layers, viz. the endoderm, mesoderm and ectoderm and accordingly designated endomorphy, mesomorphy and ectomorphy respectively. The embryological basis of the Sheldon three components of physique however has not been established. Furthermore, recent evidence indicates that this tripartite classification is not supported by statistical analysis of the correlations provided by Sheldon and that endomorphy and ectomorphy are opposite aspects of one continuum.

PARNELL, in this book, describes his own work at Oxford based on Sheldon's method of assessing body build using standardized photographs with a modification based on direct measurements. The three factors used by PARNELL are linearity of the skeleton, the relative amount of fat and muscle in the body. Components are termed fat, muscularity and linearity in place of Sheldon's endomorphy, mesomorphy and ectomorphy. Bone development is included in the estimate of muscularity. Primary dominance is indicated by capital letters, F, M, L and secondary dominance by small letters f, l and m, e.g. Lm, Lf would refer to individuals of linear build differing in relative amount of muscle and fat.

Sheldon claimed that the somatotypes described by him remained constant throughout life. However, recent work has shown that this is not true and marked variations occur depending on nutritional status, and extreme changes can occur in starvation. There is also evidence that during adult life, changes in somatotype occur, with increasing age. It is, therefore, necessary to keep constant nutritional status, physical health and age when comparing groups. The inclusion of assessments of muscle and fat in PARNELL's system is a weakness, as it has been shown by TANNER and LINDEGARD that muscularity can show considerable change in a person in a short space of time. Fat is notoriously difficult to assess and also may show marked variability in an individual within a short space of time. The only factor which remains reliably constant is linearity and it is interesting to note that factorial studies give no evidence of three components of physique but rather a bipolar factor giving linearity versus laterality.

PARNELL claims much greater correlations between physical type on the one hand and mental illness, scholastic success and other psychological attributes than most other workers. It is necessary for the findings to be confirmed by other workers before they can be fully accepted.

LINFORD REES

A. A. MASON: **Hypnotism for Medical and Dental Practitioners,** Secker and Warburg, London 1960, pp. 223, 30s.

BERNARD SHAW once observed that every worthwhile advance in medical practice tended to be

rediscovered about once every fifty years. This might well apply to the practice of hypnosis in medicine. Hypnotism has been widely known to mankind since the beginning of recorded history, and has tended to undergo alternate cycles of popular interest and studied neglect.

During the last ten years it has again come to the fore as a respectable method of treatment, although still one whose protagonists are divided between those who use it as an incidental technique in the pursuit of their general or specific aims in practice, and those who seek to make it a speciality in its own right.

Dr. MASON, author of this extremely practical monograph, writes from the point of view of an anaesthetist who discovered his own hypnotic capabilities and then found himself able to produce spectacular remission in a rare congenital skin disease, ichthyosis pigmentosa. It had not until then been thought that a constitutionally determined abnormality of the skin with strong evidence of genetic predisposition could respond to hypnotic suggestion. Since the publication of this work, and from his later experience of skin diseases, Dr. MASON has become interested in psychiatry, particularly psychotherapy, and has continued to use hypnosis as a major technique in this field.

His book covers the main uses of hypnosis in anesthesia, in psychosomatic medicine, in the treatment of psychiatric disorder, and the modification of the mental state of co-operative patients, and includes chapters on hypnosis in dental surgery and in obstetrics by two guest contributors, Mr. K. DAWSON WATTS and Dr. STANLEY D. PERCHARD. There is a succinct foreword by the late Professor ALEXANDER KENNEDY.

The outcome is a diligent, lucid, and readable treatise, comprehensive and informative, which largely succeeds in avoiding the two besetting sins of so many current books on this subject: a facile pretentiousness, sometimes amounting to tendentious grandiosity in therapeutic claims, linked to a repetitious but evasive monotony in exposition. Some of the author's own work is modestly conveyed; and it is interesting. Since the original case of ichthyosis pigmentosa, considerable exploration of the psychosomatic possibilities of hypnosis has been undertaken, culminating in recent studies of the capacity of hypnotic suggestion to inhibit or enhance specific allergic responses in selected subjects.

Hypno-anesthesia, illustrated by some impressive photographs of a mammoplasty, receives attention. Altogether this can be regarded as one of the better books about hypnosis, and as such worth a place in most students' and practitioners' library. And yet . . . and yet . . . something important is missing; despite relative comprehensiveness, an opportunity has been lost here.

Because this is a good book, and I think an honest one, it is worthwhile remarking what is lacking. All too little is effectively conveyed of the tantalising, persistently unsatisfying, aspects of hypnosis; of its capricious tendency to fail in just those cases where it had seemed most likely to succeed; to disappoint where all accepted criteria had seemed particularly promising.

The fact that there is as yet no reliable correlation between depth of trance and efficacy of treatment; that many of the most discerning practitioners find that increasing experience leads them to narrow rather than to widen the indications for its use; and that only one in four of the chosen subjects for anesthesia achieve it, and then not always consistently; these considerations cannot be disregarded in any finally complete and authoritative review of the subject.

In psychiatry, hypnosis provided Freud with the means of his first exploration of unconscious mental activity; but he abandoned it. Lindner returned to it, in the conviction that it was the one effective method of streamlining psychoanalysis; and certainly his published case histories were smoothed to classical perfection; but relapse tended to follow the ultimately inevitable cessation of intensive hypnotherapy. Even the benevolently modest but spectacularly successful Nancy School, founded by Bernheim and Liebault, did not long survive its founders.

Perhaps the historically established alternation of phases of revival and eclipse of the use and acceptance of hypnosis in medicine, is linked to the natural tendency of its protagonists to concentrate upon its undoubted potentialities, while displaying less interest in its intrinsic flaws, failures, and contradictions. Certainly these are provocative and deserve serious attention. It would be a pity if the present era of interest and recognition in the subject, exemplified by Dr. MASON's contribution, were to prove no more than yet one more positive phase of a recurrent cycle; to be succeeded once again by another period of abandonment, rejection, and neglect, the outcome of a disillusionment which only more comprehensive understanding can avert.

D. STAFFORD-CLARK

Evolution of Nervous Control from Primitive Organisms to Man, arranged by BERNARD B. BRODIE and ALLAN D. BASS, Edited by ALLAN D. BASS, American Association for the Advancement of Science, 1959 pp. 231, No price.

THE inhabitants of scientifically under-developed areas, a description which many would accept as valid for disciplines such as psychiatry and the social and behaviourial sciences, are compelled to look with admiration tinged with envy at the exciting developments in fundamental biology that are rapidly transforming biochemistry and genetics. The advances are occurring at a rate which is probably unprecedented in the history of science; the new knowledge about biological replication in the fields of genetics, protein synthesis, embryology, the multiplication of viruses and antibody formation, shows such bright promise that a synthesis of living organisms in the laboratory no longer seems a Wellsian fantasy. It cannot be long before neurology feels the impact of these remarkable developments. The possibility that the structural basis of memory is to be sought in units of a size comparable to that of the protein molecule is already under active consideration.

It is not only in the hope of vicariously sharing some of the exhilaration felt by those participating in these advances, that psychiatrists and neurologists turn their attention to them. It is often from the peripheries that the solution of important problems in a scientific discipline has come. It is perhaps wishful thinking to expect that some unifying physiological or biochemical theme can be found to link the various contributions to a volume such as this on the evolution of nervous control. Apart from a brief passage on porphyrins in the central nervous system, in PAGE's essay, the only reference to protein chemistry is in NIU's fascinating article on chemical inducers. Here the evidence that the inductor substances which direct embryonic development are probably ribonucleoproteins which may act as templates for protein synthesis is outlined.

In the essays by PROSSER and GRUNDFEST, the evolution of electrical responses of excitable tissue is traced from unicellular organisms upwards. GRUNDFEST summarises his celebrated work according to which the conduction of nerve impulses depends upon a succession of three events; the first of which is the decrementless propagation of a spike along the axon which can be initiated only electrically, the second the liberation of a chemical transmitter at the axonal termination, and the third the production of a graded potential at the input or receptor elements of the nerve cell. One doubts, however, whether we are yet within sight of defining the functional organisation of the central nervous system in electro-physiological terms.

KOELLE's essay contains an excellent summary of work on neuro-humoral agents in the nervous system and a discussion of the similarities between the endocrine and central nervous systems and the linkages between them. There are also valuable expositions of operant conditioning techniques (BRADY) and recent work on the experimental evaluation of psychoanalytic hypotheses (MIRSKY); most of the latter studies illustrate rather than verify psychoanalytic concepts. The article by TEUBER on the effects of cerebral lesions in man is a model of lucid exposition. These controlled studies of the effects of brain injuries have been carried out in such a large material that they must rank among the most valuable contemporary contributions to this difficult field. But the failure to detect any impairment of higher functions in frontal lobe lesions with the aid of objective tests is reminiscent of the pathologist who, finding no corresponding lesions in the brain, concluded that fatigue did not exist.

One had hoped for greater cohesion in a volume such as this, but it was perhaps too much to expect. It is, nonetheless, an unusually stimulating and valuable book.

MARTIN ROTH

VOL.
5
1960/6

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SERIAL BIOCHEMICAL AND ENDOCRINE INVESTIGATIONS IN RECURRENT MENTAL ILLNESS

J. H. Rey, D. R. C. Willcox, J. L. Gibbons, H. Tait and D. J. Lewis*

(*Received* 14 *July* 1960)

INTRODUCTION

Gjessing (1953*a*, *b*, *c* and *d*) can be said to be the first worker who contributed in a systematic way to a new, original and fruitful approach to the metabolic study of mental illness. His work was spread over a lifetime of patient and meticulous metabolic and clinical observations. He studied what he considered to be a well-defined group of patients, the recurrent catatonias, and with an unequalled thoroughness investigated them daily for months and years. Their behaviour was accurately observed, their psychomotor activity recorded, their environment standardised within humane limits, and balanced metabolic studies were then carried on. He found that a number of physical factors showed a definite quantitative fluctuation together with the mental state, some in phase and some with a time lag. Thus nitrogen balance showed a characteristic periodic change but the phases of positive or negative balance, though fixed in relation to the mental state in each patient, varied in time between different individuals. On the other hand, autonomic changes and fluid balance and electrolyte balance varied in phase with the changes in mental state. Other factors such as carbohydrate metabolism, liver function, vitamin utilization, etc., showed periodic oscillation.

Rowntree and Kay (1952) studied, on lines similar to Gjessing, 2 female patients suffering from recurring schizophrenic attacks. They found a number of characteristic metabolic and biochemical changes common to both patients. They only differed with regard to the nitrogen metabolism, one patient conforming more to Gjessing's type A and the other to Gjessing's type B. In both electrolyte changes bore the same relationship to the peak of an attack. There was retention of fluid, haemodilution, raised serum sodium and chlorides and lowered serum potassium up to the peak of an attack following which the trend was reversed. Decreased glucose tolerance and increased insulin resistance tended to coincide with periods of remission. Nitrogen retention varied inversely with the 17-ketosteroids output, which was highest at the peak of an attack in one patient and somewhat delayed in the other.

They concluded that the following hypothesis could account for these facts:

(1) Preceding and during the early stages of an attack a preponderance of electrolyte-controlling factor.
(2) At the height of an attack a preponderance of androgenic substances.
(3) During recovery and remissions a preponderance of "sugar active" corticosteroids.

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An opportunity arose to test partially Rowntree and Kay's hypothesis. Both of their patients were readmitted to the Maudsley Hospital at a later date and metabolic studies were undertaken. A third patient was also investigated.

METHODS

Assessment of mental state

Fig. 1 shows the method used to record the mental state. Each aspect of mentation and behaviour was assessed daily on a four point scale from the results of clinical observation and interview. In Case 1 where the more disturbed periods were characterised predominantly by excitement and the less disturbed ones by mild depression,

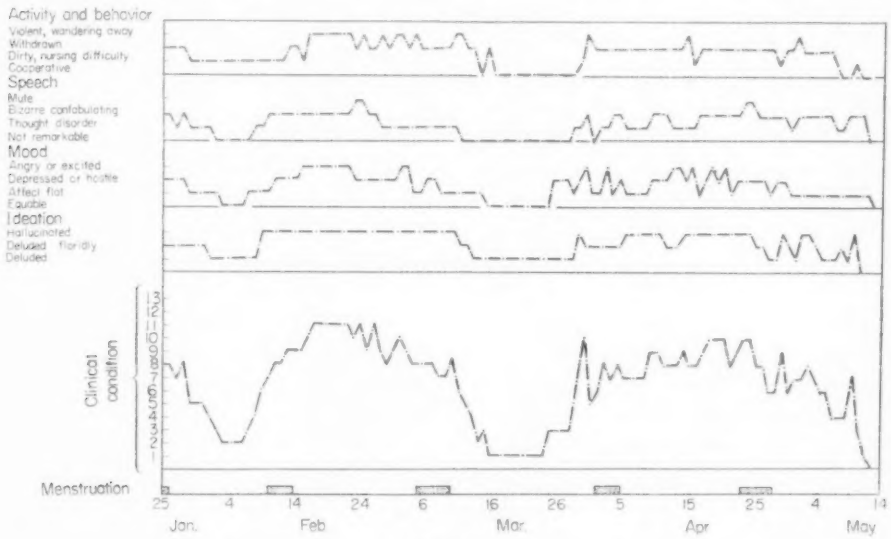

Fig. 1.

the scores have been transferred to an eight point scale with positive values indicating excitement and negative depression about a normal zero (Figs. 2 and 3). In Case 2 the total score is plotted on a sixteen point scale of increasing abnormality from a normal zero. Case 3 was similarly assessed and the degree of severity is plotted on a six point scale.

Biochemical and endocrine investigations

Vaginal smears were prepared daily in the case of Patients 1 and 2 and examined for the cornification index and for evidence of progesterone activity. The cornification index has been plotted in the charts (C.I. in Figs. 2 and 4). Weights were recorded weekly (daily in Case 3). Other serial investigations included estimation of the urinary excretion of 17-ketosteroids, acid stable formaldehydogenic substances (ASFS; corticoids), creatinine, total nitrogen, sodium and potassium. These were measured on successive 24 hr collections. Observations on serum sodium, potassium, urea, cholesterol and protein-bound iodine were also made in Case 3.

Patient 1 was intelligent and co-operative, and, retaining some insight throughout the attacks, was a most reliable collector. The values plotted and used in calculations

VOL. 5 1960/6

were those actually measured. Patient 2 by contrast was more disturbed and lacked insight. Collections were at times incomplete. All specimens containing less than 0·4 g of creatinine per 24 hr were rejected (15 per cent of urines). Sixty per cent of collections had a creatinine content of 1 g or more, with a mean of 1·2 g. All figures for other metabolites have been expressed, therefore, as values per 1·2 g creatinine. The validity of this procedure as well as the use and significance of these methods in serial investigations have been discussed elsewhere (WILLCOX 1959).

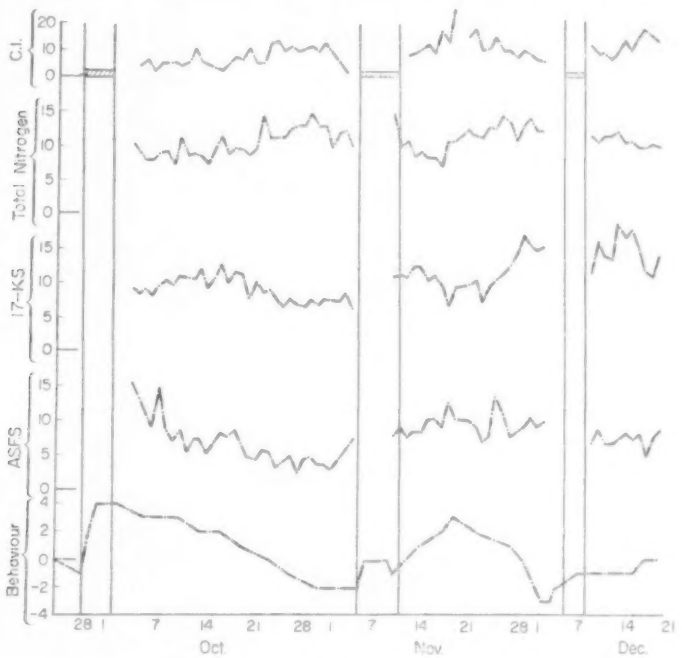

FIG. 2.

Patient 3 was co-operative in remission but in the attack collections were difficult. Careful management maintained regular complete collections with few exceptions throughout the first attack. There were however periods during the second attack studied in which satisfactory collections could not be maintained. The data for this patient are "uncorrected" but limited to the satisfactory periods.

No strict dietary control was attempted during these studies. The patients were encouraged to take a normal diet, and gross variations in food intake did not ordinarily occur in Patients 1 and 2. The composition of the diet of Patient 3 was recorded throughout although it was not possible to keep it constant.

CLINICAL DESCRIPTIONS

Patient 1 (ROWNTREE and KAY's *first patient*)

An unmarried female aged 38 had suffered from recurrent attacks of schizophrenia since age 15. The father had a markedly obsessional personality, the mother and a younger brother were normal. There was no family history of mental illness. Her childhood was normal and she did well at school. She began menstruating at 12 and her periods had been normal since. She was a sensitive girl who

blushed easily. Her first attack came at the age of 15 in 1935. She behaved in a strange way, became excited and aurally hallucinated. She had attacks of retching over meals and thought her father was going to kill her. The attack lasted 7 months. She had about twenty further attacks of mental illness, a number of them necessitating admission to hospital. In her attacks she always seemed to have been preoccupied with ideas of marriage and pregnancy. A full description is given by Rowntree and Kay (1952) of her behaviour during their investigations including some interesting psychopathology. She

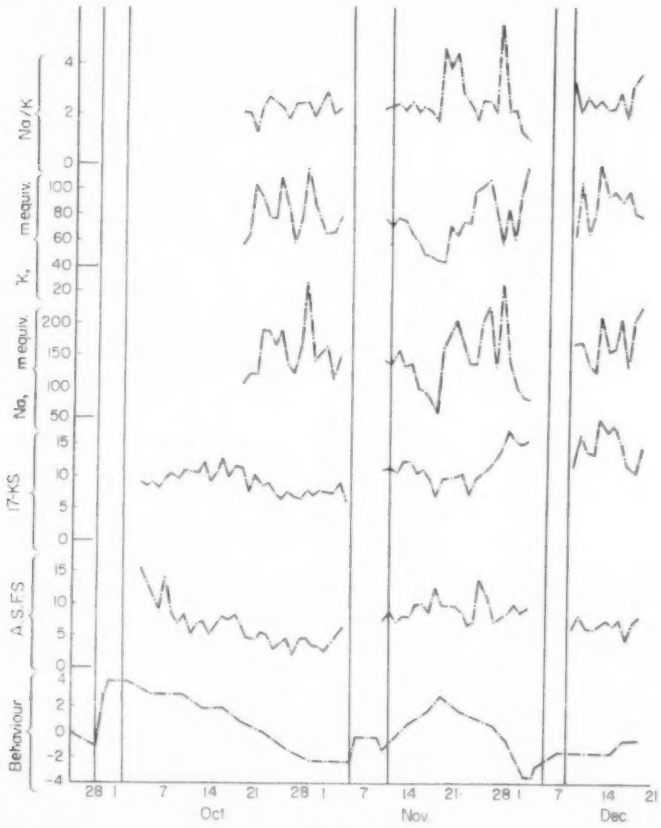

Fig. 3.

suffered from two types of attacks. During her first investigation she had three major attacks, one of 6 weeks duration, followed by a 4 week remission during which she was superficially well. The other two attacks lasted 3 weeks. During the major attacks there was a great deal of fluctuation in her mental state over periods of hours. She was hallucinated and acted out her hallucinations in postural behaviour: gleeful attitudes, tortured facial expressions, writhing of the whole body, shutting her eyes and ears with her fingers. She also neglected herself, refused food, and was incontinent at times of urine and once of faeces. Her pulse was rapid, her temperature raised and she was flushed and hot. She showed catatonic features, catalepsy, flexibilitas cerea, perseveration and extreme negativism.

The attacks during which investigations were carried out in the present study started in September 1954, and resembled the minor type of attack.

She had been given phenobarbitone and phenytoin because of the findings of episodic paroxysmal activity in the E.E.G. in relationship to attacks. At the beginning of September 1954 the dosage of these drugs had been halved. On 28th September she was seen in the out-patients' department at her request. For the preceding 5 days her sleep had been disturbed, her appetite diminished and her skin

VOL.
5
1960/6

had felt taut and her face flushed. She thought this might presage another attack and said that she felt similarly at the onset of her previous severe attack in 1949. She was slightly anxious and slightly depressed. She brought with her pieces of paper on which she had written some of her thoughts the previous night. These were grandiose, fragmentary and frequently incoherent.

The next day she became excited and began talking strangely. Her friends in the hostel thought she was a "bit queer". The following day she was admitted to hospital in a manic state. She was continuously moving about, carried a poppy in her hand, brushed her hair during interview, talked continually, for the most part coherently, with an occasional flight of ideas. She answered questions reasonably and pertinently. She was very excited and happy and slightly grandiose, expecting everyone to be greatly interested in her and to attend to her least whim. On one occasion she sobbed for a few seconds and wiped her face with toilet paper which she was carrying around. She wished to be known by her mother's name for a reason which she could not define, but had no delusions or hallucinations or schizophrenic thought disorder. She was fully orientated and performed well in tests of cognition. She described herself as being in a supercharged condition, but would not admit to having a recurrence of previous attacks.

In the course of the next 3 weeks she gradually improved. One day she said that she was convinced that the next coming of Christ would be the following Easter. On a number of occasions she exhibited thought-blocking—the only indication of schizophrenic illness occurring in this attack. Four weeks after admission her only complaint was a feeling of remoteness. This was not evident to observers and she appeared quite well.

She then became increasingly depressed, being most so in the few days preceding the onset of her menstrual period. She ate by herself, no longer enjoyed co-operating with the various tests, wept a good deal, did not want to talk in interviews, and was bored and pessimistic. She had no real ideas of unworthiness but incorrectly thought that she was in danger of losing her job.

Eight hours after the onset of her period she said she suddenly realised she was quite well. Her depression had lifted and she no longer felt remote. She was subjectively and objectively well. She remained so for 3 days and then, coinciding with the end of her period, became slightly anxious and the following day in addition slightly depressed.

She then passed into another manic state, though not so severe, as that on admission. She again had occasional thought-blocking. This again gave place to a period of depression, this time slightly more severe than the preceding one. This may have been aggravated by the coincidental holiday of her usual doctor, in whom she had confidence. She again improved considerably on the day her period commenced but remained slightly depressed. This improved progressively and she was quite well by 20th December 1956.

Laboratory studies. Figs. 2 and 3 present graphically the results from Patient 1. The vaginal smear examination showed that the first cycle was an abnormal one lasting 38 days. There was a delayed follicular phase and absence of ovulation and any well-defined progesterone effect. The second cycle was a normal one. In Fig. 2 the correlation between glucocorticoid excretion (ASFS) and mental state is clearly seen. The 17-ketosteroid (17KS) excretion follows a similar course, but there is a lag so that the peak occurs 1–2 weeks after the peak of mental excitement with which the peak of corticoid excretion closely agrees. Nitrogen excretion appears to vary inversely with the 17KS excretion. The sodium and potassium estimations were started later, and the only clearly defined changes (Fig. 3) are the steady and marked diminution in excretion during the development of the second attack, followed by a sharp rise coinciding with the peak of the attack. This attack was brief, improvement starting directly the peak was reached.

The results are summarised in Table 1 in terms of direction of changes before and after the peak of the attack.

Patient 2 (ROWNTREE and KAY's *second patient*)

A woman of 30 suffering from recurrent schizophrenia with catatonic features. The patient was the eldest of 3 children. Her father was a shy, diffident man and had had neurotic breakdowns: her mother was self-confident, over-active, ambitious and excessively concerned with her children. The patient's childhood was normal. Her illness began at the age of 15 with some inappropriate fears of pregnancy (after she was kissed for the first time). It took the form of a mild excitement with feelings of unworthiness accompanied by palpitations, malaise, and dry skin. The illness gradually worsened, she became hallucinated, her behaviour was strange and at times violent and uncontrollable. She improved gradually over the next 12 months. Two years later she had another attack and has since

Table 1.

	Before peak	After peak
Nitrogen excretion	Diminishing	Increasing
Corticoid excretion	Increasing	Diminishing
17-Ketosteroid excretion	Increasing but maximum excretion occurs after peak of excitement	Still rising but diminishing as recovery proceeds
Sodium excretion	Diminishing	Increasing
Potassium excretion	Diminishing	Increasing

Biochemical changes during attack in Patient 1.

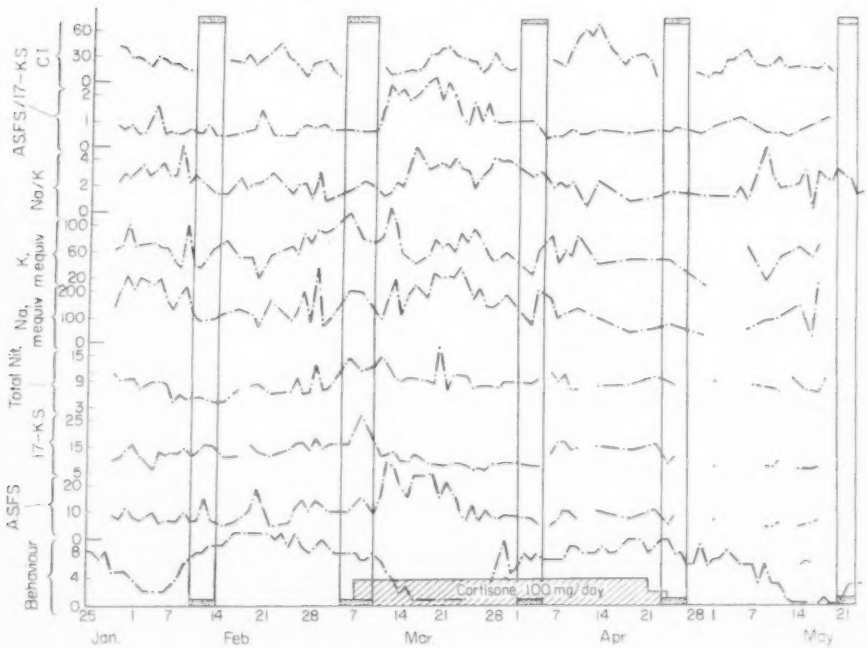

Fig. 4.

suffered from recurrent attacks of schizophrenia. In spite of insulin comas, electroshocks and prefrontal leucotomy, for the past seven or eight years her illness had assumed a definite periodicity, the duration of attacks being about 6 weeks with remissions lasting 2 weeks. Each attack followed a more or less definite pattern. There was first increasing agitation and excitement. Then she became aggressive and appeared to be hallucinated. Her behaviour was bizarre and she confabulated. Next she became withdrawn, dirty, neglected, giggling and mute. She recovered gradually from the attack passing through a paranoid phase and then became quite co-operative and friendly. Some residual abnormality was always present.

Laboratory studies. Fig. 4 presents graphically the results from Patient 2 during two attacks although four consecutive attacks were observed.

VOL. 5 1960/6

Attention is drawn first to the parallelism between the sodium excretion and the mental state. Sodium excretion is relatively low during the attacks and increased during remissions. Potassium follows a less well defined but similar course. The Na/K ratio also shows a definite parallelism with the changes in mental state, indicating that the sodium changes are predominant. This relationship appears regularly throughout the period of observation including the period of cortisone administration.

In the first cycle before interference with cortisone there is a general trend of increasing excretion of nitrogen, 17KS, and corticoids throughout the attack.

The vaginal smears prepared daily throughout show that all the cycles were normal. Cornification was normal, ovulation took place and progesterone affects were observed. Each attack covered nearly

TABLE 2.

		ASFS		17-KS		Na		K		Na/K	
		N	Mean	*N*	Mean	*N*	Mean	*N*	Mean	*N*	Mean
Before cortisone	Better	13	7·19	13	12·12	10	197·6	11	68·0	14	3·00
	Worse	15	11·71	15	16·04	17	121·4	18	78·9	20	1·86
Significance	*P*	<0·01		<0·05		<0·05		N.S.		<0·01	

exactly two menstrual cycles starting in the premenstrual phase, continuing throughout the following cycle and terminated in the next one.

For the purpose of statistical analysis all observations in the cycle before cortisone administration were placed in two groups corresponding to the phases when the patient was better and worse clinically. These phases corresponded to clinical scores of less than 6 and more than 6 respectively. These two groups of values were submitted to an analysis of variance and the statistical significance of the differences between the mean values was determined (Table 2).

Subsequently, because it was considered that some biochemical changes might be limited to or most marked in periods of clinical transition, a further subdivision was made into phases of getting better, getting worse and worse. These phases were defined as falling clinical scores from 6 to 2 (getting better), rising clinical scores from 2 to 6 (getting worse) and clinical scores of more than 6 (worse). Subdivided in this way all available values for each biochemical measure were grouped in three periods before, during and after cortisone administration. The statistical significance of the differences between the mean values was again determined, and the results are shown in Table 3.

Table 2 shows that the excretion of nitrogen, corticoids (ASFS) and 17KS is relatively low during remission and higher during the attack, whereas the excretion of sodium and potassium and the Na/K ratio are as seen in the graphs high in remission and low in the attack. The potassium differences are not statistically significant, and those for 17KS only at the 5 per cent level. Similar findings appear in Table 3. There are higher values for nitrogen, ASFS and 17KS in the worse phase, with significantly lower mean values in one or both of the other phases. The sodium differences are again significant throughout. On this subdivision the potassium differences are also significant although only at the 5 per cent level in the uncomplicated pre-cortisone period, being low in the getting worse phase and higher while getting better.

Patient 3.

This patient was first admitted in September 1954 at the age of 17:6. She was an only child. Her father, a scientist, had had several episodes of mental illness usually diagnosed as paranoid schizophrenia, although he was well between attacks. (He had typical symptoms of mania when seen in an attack here.) Her paternal grandfather had died in a mental hospital and his illness also had been diagnosed as paranoid schizophrenia. Her mother was an anxious woman and tended to be overprotective. At this time she was separated from her husband and later she divorced him.

The patient's childhood had been apparently normal. She had been to a grammar school and was thought to be of above average intelligence (I.Q. 115 on admission). She was described as happy, jolly, sociable and popular and with a tendency to daydream that did not seem excessive for an

adolescent girl. A week before admission she had been seduced by a casual acquaintance on holiday and shortly afterwards became depressed and expressed ideas of guilt and self-reproach. She was thought to be suffering from depression and seemed to be getting better until, a month after admission, she became suddenly excited. Thereafter her behaviour was very disturbed, her mood fluctuated violently, and she experienced vivid auditory hallucinations. She had numerous, changing delusions and ideas of influence. Schizophrenia was diagnosed and chlorpromazine administered. Six weeks treatment had had little effect when her symptoms suddenly disappeared at the onset of a mild febrile urinary infection. As the fever settled symptoms returned, although of less severity. They finally disappeared after a course of E.C.T. in February 1955. She was then discharged home.

Table 3.

		Getting better		Getting worse		Worse		Significance
		N	Mean	*N*	Mean	*N*	Mean	*P*
Before cortisone	N	8	9·0	7	5·1	11	7·5	<0·01
	Na	7	211·7	6	128·8	9	104·8	<0·01
	K	7	69·4	6	47·6	9	60·7	<0·05
	Na/K	7	3·1	6	2·9	9	1·9	<0·025
	ASFS	6	7·7	6	6·9	12	11·5	<0·01
	17Ks	6	11·1	6	13·0	12	10·0	<0·05
During cortisone	N	16	10·8	7	8·2	9	9·3	<0·01
	Na	16	199·0	5	181·4	12	89·7	<0·01
	K	16	72·3	5	49·3	12	48·8	<0·01
	Na/K	16	3·0	5	3·6	12	1·9	<0·01
After cortisone	N	11	8·4	5	9·5	4	10·3	<0·05
	Na	9	143·2	12	105·2	6	93·2	<0·025
	K	9	59·8	12	46·6	6	54·3	<0·10
	Na/K	9	2·7	12	2·4	6	1·9	<0·10
	ASFS	12	4·2	6	4·2	6	9·4	<0·01
	17Ks	11	8·6	6	8·3	6	13·2	<0·01

For 19 months she remained well. In October 1956, at the age of 19, she became ill again and was readmitted. This illness was the first of a series of very similar episodes which recurred at intervals of about 36 days. Each attack began abruptly: she became mute and resistive with catatonic features. After 2 or 3 days inactivity gave way to restlessness and she spoke of vague paranoid delusions and of hearing voices. Fairly rapid improvement then followed, with apparently complete recovery after an illness of 12–18 days. Her periods were irregular at this time and there was no clear relationship between them and her attacks of illness.

After the seventh episode she was transferred to the metabolic ward for biochemical investigation. There she suffered two further attacks which were longer and more severe than the others. The eighth illness began in May 1957, 36 days after the onset of the seventh. On the first day she was apprehensive, suspicious and perplexed, hinting at great events impending and at important messages which she was receiving. Consciousness was clear. She became steadily worse and on the fourth day she lay in bed inactive and almost mute. She had to be hand fed. This state continued for a week apart from one day, the third day of a menstrual period, when she seemed quite well. At this time she disclosed that she had thought that she was being hypnotized and that a Martian invasion of the Earth was in progress. President Eisenhower had been in verbal communication with her. Next day she was again mute and inaccessible. Then she gradually became more active, and often more resistive. Her movements were slow and laboured, she rarely spoke and she was given to grimacing and posturing. On the second day of the next period she was again well, for one day only. After 42 days of illness she

VOL. 5 1960/6

started to improve, with increased purposive activity. She began to talk freely and to take food without persuasion. After 48 days she appeared completely well.

The ninth attack began 72 days after the onset of the eighth. It was very similar, but lasted 70 days. Two menstrual periods occurred during this episode. There was no change in mental state during the

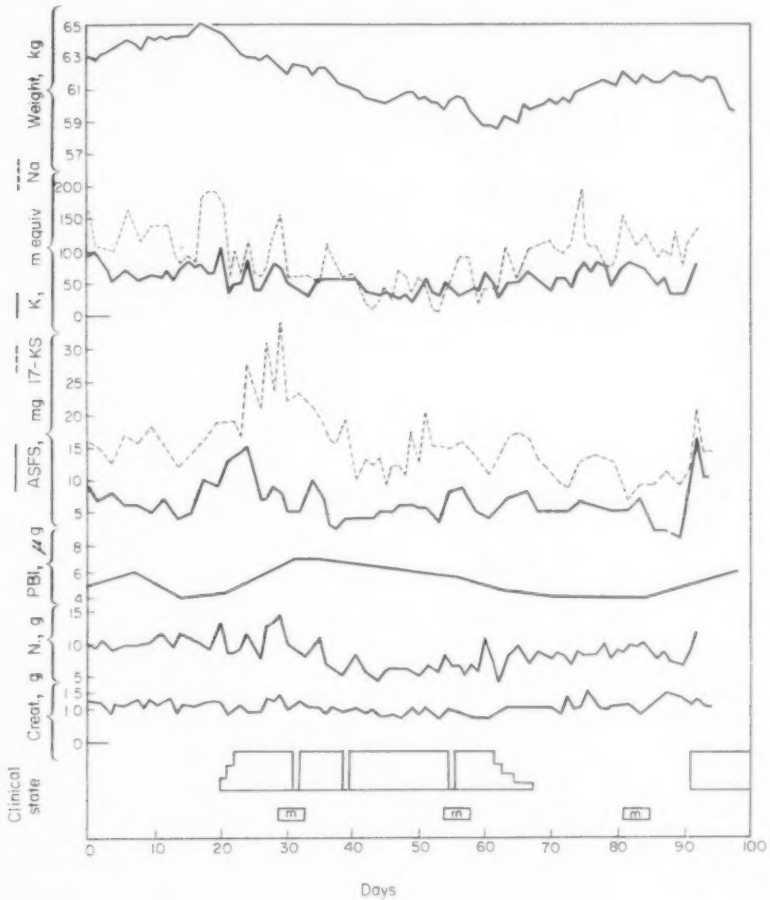

FIG. 5.

first: incomplete remission was noticed during the second and third days of the second period. She was more resistive and unco-operative during this attack and complete collection of excreta was impossible. Once again a phase of inactivity was followed by a restless phase, with eventual rapid recovery. During the latter part of this illness there was rather more variability in her mental state than usual.

When she had been well for one week, in October 1957, treatment was begun with thyroxine, 0·4 mg daily by mouth. This was gradually reduced to a regular dosage of 0·2 mg a day. She was discharged home in January 1958 and she has remained well since.

Laboratory studies. Fig. 5 shows the result of serial investigations in Patient 3 covering a period of three months, the first and last 3 weeks being remission and the intervening 6 weeks the attack. Certain changes are clearly seen. Thus there is a small but significant increase in the serum PBI at the beginning of the attack. Increases in urinary excretion of 17KS and ASFS are also seen at the onset of the reaction phase, and appear to precede the overt clinical symptoms by a few days. Nitrogen

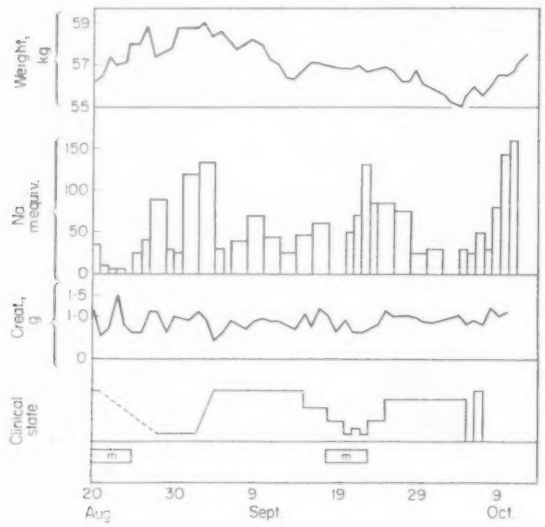

Fig. 6.

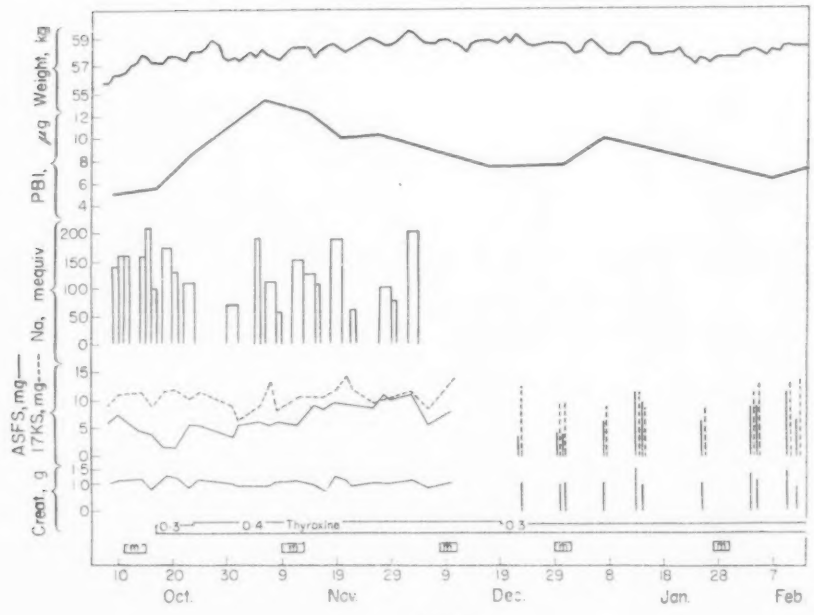

Fig. 7.

excretion does not show very marked changes. There is a rise at the onset of the attack but the excretion values then fall and are lower on average than during remission. The weight changes are striking. The steady downward trend is interrupted by the short period of remission. Sodium excretion follows the clinical course being low in the attack and higher during remission. Potassium excretion is less affected. The relationship of sodium excretion to the mental state is emphasised by the fluctuations in relation to brief partial remissions during the second attack shown in Fig. 6. By contrast in Fig. 7 following thyroxine therapy and with the patient free from symptoms all these variables follow a

much more steady course. The PBI shows changes related to the thyroxine therapy. The urinary steroids show no more than the day to day variations found in most individuals. Sodium excretion no longer shows the slow rise and fall superimposed on the daily variations. The weight and clinical state are steady. Other observations made on this patient were of the serum sodium, potassium, urea and cholesterol and of the B.M.R. Sodium, potassium and urea showed only minor fluctuations. Cholesterol tended to be high at the onset or during an attack. The B.M.R. was constantly low in remission.

DISCUSSION

It will be convenient to discuss first the similarities and differences in the present findings compared with the earlier investigation by ROWNTREE and KAY (1952) and then to consider the possible significance of the findings in the pathogenesis of these recurrent episodes.

A different relationship of the nitrogen excretion changes to the attacks of these patients has been found similar (in Patients 1 and 2) to those described in the earlier investigation, although quantitatively the changes were smaller. Thus Patient 1 had evidence of nitrogen retention at the onset of the attack, whereas Patient 2 had a period of increasing nitrogen excretion starting with the attack and Patient 3 showed reduced nitrogen excretion during the attack following a brief increase during the first few days.

It has been shown that the 17KS excretion varies in these patients, and that in general it is higher during the reaction phase than in remission, but in Patient 1 the peak of 17KS excretion was considerably later than the peak of the clinical disturbance, in Patient 2 high throughout the attack and in Patient 3 increased at onset but not maintained.

Glucocorticoid activity, as assessed by the ASFS measurements, is increased in the attack and relatively low in remission. In Patient 3 the increase was limited to the onset of the attack. This is in contrast to ROWNTREE and KAY's suggestion that the activity of these hormones was high in remission. Their suggestion was, however, based on the evidence of impaired carbohydrate tolerance and diminished insulin sensitivity. Cortisone induced changes in carbohydrate metabolism are known to persist beyond the period of increased cortisone activity, so that these changes may be misleading as an indication of the time of increased glucocorticoid activity and of course may be influenced by other factors.

Changes in sodium excretion have been consistent in all patients during both investigations.

The potassium findings appear different. The changes in serum potassium found by Rowntree and Kay were the reverse of the sodium changes, although the former were small in degree especially in their Patient 1. The urinary potassium changes presented here are similar to the urinary sodium changes, but their significance both statistically and as judged by the Na/K ratio is doubtful. If, however, an anomaly between the blood and urinary findings for potassium were confirmed it might suggest a redistribution of potassium in the body.

Regarding the biological significance of these various changes GJESSING's earlier reports laid emphasis on the periodic variation in nitrogen balance (GJESSING, 1953*c*). That these changes are not causally related to the psychotic episodes is suggested by the variable time relation to the attacks shown between GJESSING's own patients.

GORNALL *et al.* (1953) found moderate nitrogen retention associated with the reactive phase in 2 of 3 patients studied. HARDWICK and STOKES (1941) abolished the periodic nitrogen fluctuations in one patient by increasing the protein intake but the attacks continued.

Apart from diet, nitrogen excretion is affected mainly by androgen (anabolic) and glucocorticoid (katabolic) activity, and oestrogens may also have some action. It is therefore difficult in a cyclical condition in which all three of these hormone groups are varying to predict the behaviour of nitrogen excretion. In Case 1 nitrogen excretion appeared in the main to vary inversely with 17KS excretion, suggesting that an androgen anabolic effect was dominant. In Case 2 nitrogen excretion increased throughout the attack as did the urinary ASFS suggesting a dominance of glucocorticoid katabolic action. In Case 3 the initial increased excretion might be attributed to corticoid activity, but during the remainder of the attack the nitrogen excretion fell and was at a lower level than in remission, due in part at least, to the reduced food intake. Further, as a change in nitrogen metabolism would call on a compensatory homeostatic increase of the regulating hormones it is not possible to state which is the primary process and which the secondary or compensatory one. Nitrogen changes therefore are not constant and may be the result of several factors known to vary with these attacks.

The changes reported in steroid excretion are also of varied kinds. Of the present cases one has maximal corticoid excretion at the height of the illness followed by a peak of 17KS excretion, the second shows a rise of both these steroid fractions together throughout the attack and the third an initial increase which was not maintained throughout. Gornall *et al.* (1953) reported one patient with little evidence of steroid fluctuations and another with high 17KS excretion, especially at the onset of attacks, and normal corticoid excretion (formaldehydogenic substances). There may be many reasons for fluctuations in steroid excretion. It is known that excitement, anxiety and agitation increase corticoid excretion, and therefore increases are to be expected in so far as these emotions are features of the reaction phase. It is of interest in this connexion that the expected increase in corticoid excretion initially present was not maintained during the whole period of cortisone administration in Case 2. This probably indicates a change in the metabolism of cortisone during the persistent abnormal load, and one wonders whether it might also imply some minor abnormality in the metabolism of endogenous 17-hydroxycorticosteroids. Factors influencing androgen activity are less well understood, but it is possible that mental events with a sexual content or significance may be associated with increased androgen excretion (Gibbons *et al.*, 1960). Thus both the nitrogen and the steroid changes may be explained as reactive to the mental disturbance. It is of course possible to argue that there are basic rhythms in these hormonal activities and that this is one determinant of the mental state, although there is nothing in the data to demand this direction of argument. Rey (1957) has added to this view suggesting that recurrent or periodic disturbances may result from a failure of maturation of the normal hormonal and perhaps other metabolic interrelationships so that individual functions rise and fall without achieving a satisfactory balance or homeostasis. The functional disorders of menstruation provide a parallel. Whichever the direction of events, psychic to somatic or vice versa, this concept of an underlying failure of maturation with repeated attempts by the organism to reach a different level of psychophysiological organisation can still apply and with further knowledge may have therapeutic implications.

As shown in Patient 2, cortisone in doses of 100 mg daily for 2 months did not alter the course of the illness. Treatment with thyroxine has also been tried in periodic

VOL.
5
1960/6

catatonia. It was first given with the idea of reversing nitrogen retention and so preventing the attack. However the relationship between nitrogen metabolism and cyclic mental changes stressed by Gjessing does not seem to be of primary importance, as mentioned above. Nevertheless several authors (GJESSING, 1953*d*; DANZIGER and KINDWALL, 1954) have claimed that thyroxine treatment leads to remission in some cases of periodic catatonia or recurrent schizophrenia. Patient 2 was treated with thyroxine only to relapse after initial improvement (ROWNTREE and KAY). Patient 3 was given thyroxine during remission from an attack and she has remained well for two and a half years since. By contrast with Patient 2 who received large doses of thyroxine and thyroid extract, she remained well on average doses of thyroxine. Doses of 0·4 mg raised the serum PBI to around 12 μg per 100 ml but the dose was then reduced so that the PBI level remained within the upper part of the normal range. She was maintained on 0·2 mg per day.

None of these patients had any direct evidence of thyroid dysfunction, although all had low B.M.R.s, Patient 2 persistently (−15 to −40 per cent) and Patient 3 only during remission (−20 to −30 per cent).

We know of no convincing rationale for this treatment, but the seriousness of the illness in Patient 3 and the poor prognosis suggested by the lengthening of the attacks give grounds for believing that the cessation of attacks might be due to the treatment. Consequently the patient was advised to continue taking thyroxine indefinitely. After two and a half years she remains well, is now married and has a child.

A decrease in sodium excretion during attacks of recurrent schizophrenia and in the depressive phases of manic-depressive illnesses has been reported by several workers (GJESSING, 1953*c*; KLEIN and NUNN, 1945; CRAMMER, 1959; STRÖM-OLSEN and WEIL-MALHERBE, 1958). A similar decrease was found during the attacks of our patients. In Patient 1 potassium excretion follows the same pattern as sodium. In Patient 2 the diminution of potassium excretion is greatest at the onset of an attack. In Patient 3 it follows the same pattern as sodium but is less marked. The influence of diet on such changes must obviously be considered. With Patients 1 and 2 food intake was well maintained during the attacks. Moreover in Patient 2 potassium excretion began to increase before that of sodium. Further ROWNTREE and KAY (1952) found similar sodium changes when these two patients were receiving a fixed diet. With Patient 3 a moderate fall in calorie intake occurred a few days after the onset of the attack, but the marked fall in sodium excretion had preceded this. GJESSING (1953*c*) demonstrated similar fluctuations in balance studies. Dietary changes are therefore not the whole explanation. In the present study fluctuations in corticoid excretion accompanied the urinary electrolyte changes. However the rhythmical changes in sodium excretion continued during the administration of cortisone to Patient 2, although retention of fluid occurred as shown by an increase in weight. Factors other than endogenous cortisol secretion must therefore have contributed to the fluctuations in sodium excretion. Aldosterone might be the immediate determinant but its role has yet to be elucidated. The possibility of a redistribution of electrolytes in the body fluids has some support in two other studies. GIBBONS (1960) found that total exchangeable sodium was greater during depressive illnesses than after recovery. COPPEN (1960), in studies of the blood-brain barrier, found a decrease in the rate of entry of radio-active sodium into the C.S.F. in depressed patients.

The interest of these findings is that brain activity is closely related to sodium and

potassium metabolism. Changes in electrolyte metabolism in the brain might afford an explanation for changes in mental state. The work of Woodbury (1954, 1958) on the regulation of brain excitability via the hormonal control of brain electrolytes and the redistribution of sodium ions is of considerable relevance, as it may be suggestive of the mechanism at work in these cases.

SUMMARY

(1) Three patients with recurrent mental illness were investigated. Serial biochemical observations were made.

(2) It was demonstrated that recurring variations in nitrogen, sodium, potassium, corticoid and 17-ketosteroid excretion took place in connection with the behaviour changes.

(3) Changes in mental state and in metabolism occurred simultaneously and it is extremely difficult to define cause and effect.

(4) One patient remains free of attacks for 2 years whilst receiving thyroid therapy.

(5) Reasons are given for believing that many of the changes described are reactive, but that the regular fluctuations in sodium excretion with mental changes may reflect a direct pathogenic process.

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OL.
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STUDIES ON SALIVARY FUNCTION IN MAN: VARIATIONS IN SECRETORY RATE AS PART OF THE INDIVIDUAL'S ADAPTIVE PATTERN*

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(*Received* 4 *August* 1960)

IT HAS been demonstrated that various bodily functions are altered when the human organism is placed in a situation which is interpreted as adverse or threatening (WOLFF *et al.*, 1949). In several organ systems, two patterns of alteration have been delineated: hyperactivity and hypoactivity. It has been maintained that the type of change that developed (either hyper- or hypoactive) is related both to the significance of the specific threatening situation to the individual and to the individual's more general pattern of dealing with day to day problems (WOLFF, 1949). The studies reported here are concerned with alterations in the salivary flow in man that occur following the presentation of a threatening stimulus, and the relationship of these changes in flow rates to the adaptive pattern of the individual.

The well known studies of animals by PAVLOV (1910) provide abundant data on the relationship of central nervous system activity to salivary flow. Comparable conditioned reflex studies in man have been cited in the Russian literature (KASATKIN, 1952). Other studies in man which have focused on salivary function in relation to central nervous system activity include those of WINSOR on the effects of mental effort (1931); of STRONGIN and HINSEY (1938*a*, *b*) in various psychotic states; of WOLF and WOLFF (1943) on the subject Tom in regard to affect change, and finally the work of SZASZ (1950) based on the clinical reports of his patients undergoing psychoanalysis. It has been the purpose of our studies to observe the quantitative changes in the rate of salivary flow that occur in a series of normal individuals when placed in a situation interpreted as threatening. In addition, we have attempted to relate these changes to the more general behavioral characteristics of the individual as assessed by a partially-focused and partially open-ended interview carried out after the stress period but without knowledge of the results of measurements of salivary flow.

METHODS

Measurement of the rate of salivary flow

A two-chambered disc such as that designed and described by LASHLEY (1916) was applied to the opening of the parotid duct on one side (Fig. 1, A and B). The outer chamber, through a connection to water flow suction, was used to attach the disc firmly to the buccal mucosa at the periphery of the duct orifice. The inner chamber was placed directly over the stoma of the duct, and saliva was allowed to run by gravity into a rubber tube, from which drops of fluid fell freely. The rate of flow was measured by the number of freely flowing drops per min. The jaw was usually open during the measurements, and opening and closing movements were made only two or three times during an experiment.

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VOL. 5 1960/6

At the beginning of each experiment, the rate of flow of saliva was allowed to stabilize after instrumentation due to the introduction of the apparatus into the mouth. Measurements of the rate of flow were then made for three 3-min periods: before, during, and after the presentation of the threatening stimulus.

Stimulus

The imminence of tooth drilling in the dental chair was selected as an appropriate threatening stimulus. It is generally interpreted by most subjects as an unpleasant situation, and is often accompanied by tension and anxiety. The validity of such a choice was borne out by the fact that all but one of the subjects (see notation later in the text) of this study stated that the experience was highly disagreeable. The drill was started and brought toward the mouth, but no actual drilling was conducted. The patients described their affect in the following terms: ". . . one of apprehension . . .", ". . . very unhappy . . .", ". . . I dread dentists . . .", ". . . afraid . . .", ". . . hold no love for it . . .", ". . . it upsets me a great deal . . .", etc.

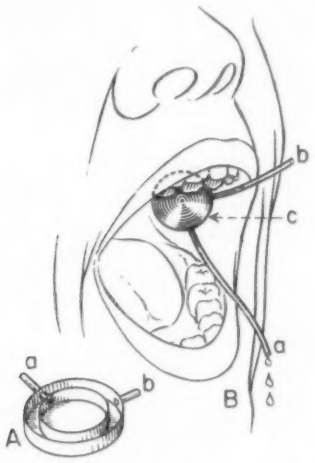

FIG. 1.—A. Saliva collection cup; a. drainage tube for saliva; b. tube for suction attachment; B. saliva cup, c. in place in mouth.

Interview technique

Each subject was interviewed for an hour or more by one observer (S. W.) at a time and place removed from the experimental day and situation. The interview was conducted independently of any knowledge of the salivary flow measurements. The interview was recorded and heard independently by another member of the group (M. D. B.). The interview consisted mainly of a biography of the subject. Inter-actions with parents and colleagues were focused upon, as well as reactions in the situations of work, schooling, family raising, etc. Special note was made of whether the individual's characteristic pattern of meeting challenges in the past was of an assertive and forceful nature, involving aggressive, decisive and frontal attack actions, or of a defensive nature, involving immobility, evasion or non-participation. These two patterns of reaction were characterized accordingly as aggressive and defensive. The ratings of these patterns were agreed upon by both interview reviewers prior to a study of the salivary flow data. In addition, each subject was questioned concerning his past awareness of salivary changes during periods of a threatening nature.

Subjects

Twenty-four subjects were studied, 17 females and 7 males in the age range 14–65 years. All subjects had been in the same dental office many times previously. The observations were made during a routine dental appointment that had been scheduled as part of their necessary dental care.

The patients had been informed on a prior visit that saliva would be collected, and they had seen and had become familiar with the apparatus prior to the actual study day.

RESULTS

Table 1 lists the 24 subjects and the salivary flow rates for the control and subsequent stimulus and post-stimulus periods. The subjects have been divided

TABLE 1.—GROUP A—"AGGRESSIVE"

Subject Age, Sex	Control	Salivary flow rates (drops/min) Stimulus	Salivary flow rates (drops/min) Post stimulus	Previous sensation*
1. R. G., 40 F	2	22	5	W
2. A. A., 50 F	1	7	1	N
3. N. W., 21 F	1	15	2	W
4. M. B., 22 M	6	24	4	W and D
5. M. B., 52 M	2	11	1	W and D
6. S. D., 23 F	2	7	2	W and D
7. R .S., 20 F	4	23	3	D
8. C. G., 42 F	1	6	1	W
9. G. R., 20 F	2	7	2	W
10. M. C., 45 F	1	8	1	N
11. J. C., 20 F	3	19	2	N
12. M. O., 32 F	1	10	0	N
13. S. I., 65 M	2	2	1	N
14. N. G., 45 M	0	4	0	N
15. J. N., 46 F	2	11	1	W
16. A. G., 48 F	3	6	1	N
17. N. W., 42 M	1	11	1	W and D
Mean	2·0	11·4	1·7	
S.E.	0·5	1·7	0·5	
Sig.		$P < 0{\cdot}01$	$P < 0{\cdot}01$	

GROUP B—"DEFENSIVE"

18. B. J., 15 M	2	0	0	W and D
19. M. L., 45 F	3	0	1	D
20. M. G., 32 F	2	0	0	D
21. A. G., 49 F	4	14	6	D
22. S. K., 25 F	3	0	1	D
23. S. N., 20 M	3	0	0	D
24. D. R., 14 F	3	0	1	N
Mean	2·9	2·0	1·3	
S.E.	0·3	2·0	0·8	
Sig.		$P < 0{\cdot}01$	$P < 0{\cdot}01$	

* W = wet, D = dry, N = none recalled.

Statistical analysis—Group A vs. Group B

Control: not significant

Stimulus: $P < 0{\cdot}01$

Post-stimulus: not significant

VOL. 5 1960/6

into groups A (aggressive) and B (defensive), and a notation is made of the previous salivary flow changes recalled by the patient. The change in flow, increase for Group A and decrease for Group B, during the stimulus period is significant for both groups at the $P < 0{\cdot}01$ level. The rates for both groups during the control periods are similar, but the rates during the stimulus period are significantly different from each other ($P < 0{\cdot}01$).

DISCUSSION

Three types of alteration to a threatening stimulus were observed in this study: an increase, a decrease and no change. The one individual (S. I.) who illustrated the no change type of response was rated as having used aggressive patterns of activity in dealing with day-to-day problems. This subject was a successful corporation lawyer and prominent political figure in the community. He reported that the dental chair situation was not threatening to him. On the contrary, he considered it a welcome respite from the pressing duties of his office; he described it as "relaxing . . . a chance to merely sit back and not work . . ."

In the 23 other subjects, either a fairly marked rise occurred or a sharp cessation of all flow. These response patterns of hyperactivity and hypoactivity appear to be related to the type of past behavior pattern of the individual, although in Group B subject A.G. demonstrated a rate response in a direction opposite to the rest of the group. The rate responses do not correlate well with the subject's recall for previous salivary flow changes during stressful situations. The neuro-endocrine basis for the differentiation of these observations may depend upon the neurophysiology of the parotid gland which contains only serous cells. It receives its sympathetic innervation by way of branches accompanying the blood supply, and its parasympathetic from the inferior salivary nucleus by way of the glossopharyngeal nerve which traverses the otic ganglion and then penetrates the gland. Animal studies have indicated that stimulation of the parasympathetic supply results in a brisk secretion from the parotid. Sympathetic stimulation has not effected the same increase in flow; but neither is there evidence that sympathetic stimulation decreases the rate of flow of a parasympathetic-stimulated gland. Thus, no clear-cut antagonism between the two divisions has been demonstrated, although one is more effective than the other in increasing the rate of flow.

For all but one of the subjects (S. I.) the dental chair situation was perceived as threatening. The two predominant types of responses are related to the behavioral pattern of the individual as assessed by the interview. Although this type of psychological and personality profile inventory has not been standardized for many different laboratories, in our studies it did afford a behavioral assessment of the subject. The fact that there is such a striking physiologic correlate appears not to be a chance phenomenon; and although this correlation does not confirm the validity of the personality assessment, it does project it into a meaningful biologic context.

The potential biologic purpose of increased salivation is not clear; but as part of an aggressive approach to a threat the increase may relate to the general increased mobilization of energy that characterizes the aggressive type of behavioral response. The decrease in flow may be viewed as part of the relative immobility and restraint of energy release of the defensive reaction.

To view these different patterns in light of the neurophysiologic studies reviewed

above, one might speculate that the aggressive response is accompanied by parasympathetic stimulation and that the defensive reaction is not. It is not known whether there is any specific inhibitory factor. One cannot indicate that activation of the sympathetic supply to the parotid gland is responsible for this failure of secretion, although it is a familiar fact that epinephrine and atropine, as well as anticholinergic agents, induce dryness of the mouth.

SUMMARY

(1) Salivary flow rates have been observed in 24 subjects before, during and after the presentation of a threatening stimulus in the form of imminent dental drilling.

(2) Interviews were conducted without knowledge of the results in an attempt to assess the general behavioral patterns of response of the subjects to life situational problems.

(3) Those individuals whose patterns were rated as aggressive were more likely to demonstrate increases in salivary flow; those whose patterns were defensive were more likely to demonstrate a decrease.

(4) The possible neurophysiologic mechanisms and the biological significance of the changes is discussed.

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VOL.
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1960/

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A SURVEY OF THE RELATION BETWEEN CERTAIN COMMON ANTENATAL COMPLICATIONS IN PRIMIPARAE AND STRESSFUL LIFE SITUATIONS DURING PREGNANCY*

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INTRODUCTION

IN RECENT years there have been several reports of psychosomatic studies of patients with the common antenatal complications of pregnancy—prolonged labour (CRAMOND, 1954), toxaemia of pregnancy (COPPEN, 1958) and severe vomiting in early pregnancy (COPPEN, 1959). These investigators have also reviewed the scanty but suggestive evidence of a relation between stressful life situations, personality factors and the occurrence of these conditions. No attempt to duplicate these reviews will be made here. However, the evidence was considered sufficiently suggestive to warrant further investigation.

In this paper the results are reported of a preliminary survey of the incidence of stressful life situations in a group of primiparae with three common antenatal complications compared with a group of normal primiparae. It was naturally of interest to compare the findings from an Australian series with the previous studies from the United Kingdom. However, it will not be possible to make comparison on all points because the present investigation was initiated prior to the publications by COPPEN (1958, 1959).

One particular point of interest in this investigation was the opportunity provided by the large post-war migration to Australia to compare the incidence of these various complications in "new" Australian patients with Australian born patients.

METHOD

The investigation was confined to patients in their first pregnancy. The patients were interviewed in a quiet room by one of us (B.B.), a married female social worker, between the fifth and ninth day of the puerperium on one occasion only. The information was obtained in 50–90 min in most cases but in an occasional uncommunicative patient more time was taken. The information was recorded on a specially drawn up protocol at the time of the interview. After this the data obtained was transferred to a punch card specially devised for the purpose and tabulation was made from these cards.

Consecutive cases were used as far as possible except when selection was demanded either because of a language barrier, stillbirths, illness in the puerperium which

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precluded a long interview, or a refusal on the part of the woman herself. The language barrier was responsible for most of the deviations from a consecutive series.

The groups of cases conformed to the following criteria:—

Normal group (54 patients). In all these cases the course of pregnancy and labour was normal. Two of the patients had minor medical complications, namely mumps at eight months in one and morbilli in the other.

Prolonged vomiting group (30 patients). Cases in this group were those where vomiting rather than nausea was still troublesome during and beyond the fifth month of pregnancy.

Toxaemia of pregnancy group (40 patients). Hospital admission for treatment of toxaemia was the first criterion. Those cases who responded rapidly to rest and

TABLE 1.—AGE INCIDENCE, MARITAL STATUS, RELIGION AND BACKGROUND OF FOUR GROUPS

	Normal	Prolonged labour	Prolonged vomiting	Toxaemia
Number of patients	54	44	30	40
Not booked	1	5*	2*	8†
Not married	9	9	2	9
Under 20	15	13	7	11
Over 30	2	7	2	5
Roman Catholic	10	14	15†	10
Non-Australian parents	16	19	12	13
Non-Australian husband	19	27	14	15

* $P < 0{\cdot}05$.
† $P < 0{\cdot}01$.

sedation and proceeded uneventfully to term with spontaneous labour were not included in this study. The cases included were those who failed to respond to rest and sedation as indicated by persistence of elevated blood pressure, oedema or albuminuria. Eclampsia occurred in 7 patients. Induction of labour had to be carried out in 16 cases while Caesarean section was undertaken in 7 others. Cases of essential hypertension or renal disease were excluded.

Prolonged labour group (44 cases). Cases in this group were those who were in *continuous* labour for more than 24 hr.

Both prolonged labour and toxaemia occurred in 5 patients, prolonged vomiting and prolonged labour occurred in 6 patients, while prolonged vomiting and toxaemia occurred in 2 patients.

RESULTS

(1) *Age, bookings, parents, religion, birth place*

No significant differences were apparent between the ages of the control and any of the three abnormal groups. As might be expected the incidence of unbooked patients rose in the abnormal groups as the hospital has received such emergencies for many years (Table 1).

Although there was a higher incidence of patients with non-Australian parents in the prolonged vomiting and prolonged labour groups this did not reach statistical

VOL. 5 1960/6

significance. Neither was the incidence of those of Northern European birth significantly different in any of the groups. There was a rather low incidence of Southern Europeans (8 per cent) in all groups this was probably due to the language barrier.

There was, however, a higher incidence of patients of the Roman Catholic religion in the prolonged vomiting group compared with the control and toxaemia groups ($P < 0.01$). The incidence of Roman Catholics in the normal group is in accordance with recent census figures. The overall incidence of Roman Catholics in all three complicated groups was twice that in the normal group. This difference just failed to be significant at the 5 per cent level ($P < 0.055$).

TABLE 2.—INCIDENCE OF SYMPTOMS BEFORE AND DURING PREGNANCY

	Normal	Prolonged labour	Prolonged vomiting	Toxaemia
Number of patients	54	44	30	40
Symptoms before pregnancy				
Emotional	19	25	11	21
Bodily	2	13†	10†	10*
Number of patients‡	39	42	27	36
Bodily symptoms during pregnancy (Two or more)				
Mid trimester	29	20	15	20
Last trimester	26	29	16	28

* $< P\ 0.05$ | † $< P\ 0.01$ | compared with normal group.

‡ Information on symptoms before pregnancy was not available in all subjects.

(2) *Incidence of symptoms prior to and during pregnancy*

There was a significantly higher incidence of bodily symptoms prior to pregnancy in all three abnormal groups. These symptoms included mild digestive disturbance, palpitation, tremor, excessive sweating and headaches. There was however, no difference in the incidence of emotional disturbance such as depression, tension and apprehension in the abnormal groups compared with the normal group (Table 2).

There was a high incidence of patients with two or more bodily symptoms (approximately 50 per cent) during pregnancy in all groups—the incidence increased in the last trimester to almost 75 per cent in the prolonged labour and toxaemia groups. These symptoms included headaches, insomnia, fainting, swelling of feet, frequency of micturition or indigestion. The various groups did not however differ significantly in the incidence of such symptoms.

No differences were apparent in the birth place of patients with and without symptoms prior to pregnancy.

(3) *Incidence and type of stressful life situation during pregnancy and relation to symptoms*

It is of interest that over half the control patients reported stressful life situations (Table 3). However, the number of stressful life situations reported by the patients with prolonged vomiting and toxaemia was quantitatively greater ($P < 0.001$). The increased number reported by patients with prolonged labour just failed to reach

statistical significance ($P < 0.06$). Analysis after removal of the stressful effect of the complication itself confirmed the significance of the differences between the controls and the prolonged vomiting ($P < 0.01$) and toxaemia groups ($P < 0.02$) (Table 3).

These stressful situations occurred within a month of the occurrence of symptoms during pregnancy in approximately half of the prolonged vomiting group and two-thirds of the toxaemia group.

TABLE 3.—NUMBER OF STRESSFUL LIFE SITUATIONS IN PREGNANCY (EXCLUSIVE OF COMPLICATIONS THEMSELVES)

	No. of patients	Number of situations						
		0	1	2	3	4	5	Total
Normal	54	26	21	5	2	–	–	28
Prolonged labour	44	14	18	8	3	1	–	30
Prolonged vomiting	30	7	8	8	3	2	2	23*
Toxaemia	40	10	16	7	3	4	–	30†

* $P < 0.01$ compared with normal group.
† $P < 0.02$ compared with normal group.

TABLE 4.—TYPES OF STRESSFUL LIFE SITUATION

	Normal	Prolonged labour	Prolonged vomiting	Toxaemia
Number of patients	54	44	30	40
Pregnancy itself	16	21*	13	17
Interpersonal	6	8	12‡	14†
Economic	—	5*	8‡	9‡
Occupational	1	4*	3*	6†
Complications	1	8†	12‡	17‡
Other	14	10	15*	8
Totals	38	56	63	70

* $P < 0.05$ compared with normal group.
† $P < 0.01$ compared with normal group.
‡ $P < 0.001$ compared with normal group.

Analysis of the type of stressful life situation in the various groups revealed a significant incidence of the pregnancy itself only in the prolonged labour patients (Table 4). Interpersonal difficulties were more evident in the other two groups. All three abnormal groups showed a higher incidence of economic and occupational factors than the normal group. As would be expected the complications themselves were a source of stress in all three abnormal groups (Table 4).

(4) *Attitude to pregnancy*

The attitude of the patient to pregnancy was sought before, during and afterwards. An increased incidence of rejection before pregnancy was noted in all three abnormal groups when compared with the control group, but this did not reach statistical significance (Table 5). During pregnancy a higher incidence of unfavourable or indifferent reactions was noted in the prolonged labour group and in the toxaemia group compared with the normal group and the prolonged vomiting group ($P < 0.01$).

VOL. 5 1960/6

A similar significant incidence of unfavourable reactions was noted after pregnancy in the prolonged labour and toxaemia groups.

Some indication of attitude to the pregnancy can be gained from the figures for attendance at preparatory lectures and relaxation classes. It was of interest that attendance at lectures fell markedly in the prolonged labour group and the prolonged vomiting group compared with the control group and the toxaemia group ($P < 0.01$).

TABLE 5.—ATTITUDE TO PREGNANCY

	Normal	Prolonged labour	Prolonged vomiting	Toxaemia
Number of patients	54	44	30	40
Before pregnancy:				
Rejection	18	20	14	17
During pregnancy:				
Rejection then acceptance	8	11	10	7
Unfavourable or indifferent	13	22†	10	20†
Acceptance followed by rejection	8	7	5	11*
After pregnancy:				
Unfavourable	13	19*	9	20†
Non-attendance at preparatory lectures	9	17†	13†	11
Non-attendance at relaxation classes	9	17†	12†	12

* $P < 0.05$.
† $P < 0.01$.

A similar incidence was noted with attendance at relaxation exercise classes. There was a higher incidence of patients of non-Australian parentage in the non-attenders in these two groups ($P < 0.05$).

(5) *Attitude of the husband*

The husband was considered an inadequate provider in a significant number of toxaemia patients compared with the other groups ($P < 0.05$). There was also a higher incidence of rejection by the husband after pregnancy in the toxaemia group compared with the other groups ($P < 0.01$).

No differences in the husband's occupation or social class were apparent in any of the abnormal groups compared with the normal group.

(6) *Attitude to sex, menstruation and contraception*

No differences in attitudes to menstruation, sexual intercourse, or contraception were noted in the various groups. Neither were differences apparent between patients of non-Australian parentage and those of Australian parentage. The incidence of dysmenorrhea was 33 per cent in the control and prolonged labour groups, 35 per cent in the toxaemia group and 43 per cent in the prolonged vomiting group. These differences were not significant.

Satisfactory sexual adjustment with the husband was claimed by 30 of 54 (55 per cent) in the control group, 24 of 44 (54 per cent) in the prolonged labour group, 22 of 30 (73 per cent) in the prolonged vomiting group and 26 of 40 (67 per cent) in the toxaemia group. These proportions did not differ significantly.

Contraception was practised by only one quarter of each group.

(7) *Abnormalities in the mother's obstetric and medical history*

There were no significant differences apparent in the mother's obstetric history. There was no evidence of an undue incidence of hypertension in either parent nor were there any significant differences in the medical and obstetric history of the siblings.

(8) *Dietary history*

Information on the dietary intake was obtained at the time of interview in all patients. No different incidence of dietary inadequacy was noted in the abnormal groups from that in the control.

DISCUSSION

A higher incidence of stressful life experiences was found in patients with prolonged vomiting and toxaemia when compared with the normal group. It is difficult to be certain about the significance of this finding. It is possible that patients with these complications would be more likely to recall stressful life situations than the control group. However, the high incidence of such situations in the control group weighs somewhat against this interpretation. It is of interest that the type of stressful life situation differed somewhat in the normal and abnormal groups. A higher incidence of stress due to the pregnancy itself occurred in the prolonged labour group while a higher incidence of interpersonal difficulties was noted in the prolonged vomiting and toxaemia groups. An increased incidence of economic and occupational factors was noted in all three of the abnormal groups.

The evidence of stress was greatest in the patients with prolonged vomiting. However, no evidence of disturbed sexual function was obtained in these patients as previously reported by COPPEN (1959) in patients with severe vomiting in early pregnancy. Evidence of rejection of pregnancy might be indicated by the incidence of non-attendance at lectures. However, the symptom itself may have kept the patients at home and there was no evidence of unfavourable reaction during or after pregnancy in contrast to the patients with prolonged labour or toxaemia. However, this finding is subject to the limitation of the retrospective nature of the study. These patients may have quickly lost or denied feelings of rejection that they may have had during pregnancy. There was a significantly higher incidence of bodily but not emotional symptoms prior to pregnancy. These patients also showed a higher incidence of the Roman Catholic religion though they did not come from a significantly higher non-Australian parentage.

The high incidence of stressful life experiences in patients with toxaemia of pregnancy has also been reported by COPPEN (1958). It is of interest that COPPEN found emotional disturbances in these patients to be particularly associated with their families. The finding of a high incidence of interpersonal difficulties in the present study substantially confirms this observation. A significant incidence of bodily symptoms was noted prior to pregnancy but no undue incidence of sexual maladjustment or premenstrual tension was encountered in these patients as found by COPPEN in

VOL.
5
1960/6

his series. However, evidence of rejection of the pregnancy by the husband was evident. The husband was also an inadequate provider in a significant number of cases. The pregnancy was viewed unfavourably during and after its course by these patients though as above this finding is subject to the limitations of the retrospective interviewer. However, there was no undue incidence of non-attendance at lectures or exercises in this group in contrast to the other two abnormal groups. COPPEN (1958) found evidence of a significantly less welcoming attitude to the coming baby in his patients with toxaemia.

In the patients with prolonged labour there was also evidence of a higher incidence of bodily symptoms prior to pregnancy. There was significant evidence of unfavourable reactions both during and after pregnancy had been completed—a finding again subject to the limitations of the retrospective interviewer. Further evidence of rejection of pregnancy was provided by the high incidence of non-attendance at lectures and exercises which patients should have been able to attend. There was a higher incidence of patients of non-Australian parentage in the group of non-attenders. An undue incidence of sexual difficulties was not admitted by these patients though CRAMOND'S (1954) previous observation of a high lie score in these patients must be borne in mind. CRAMOND'S finding of an undue incidence of peptic ulcer in this group was also not confirmed in the present series.

An unexpected result was the absence of differences in attitudes to menstruation, sexual intercourse and contraception. Now it must be readily admitted that patients may well not reveal their true feelings especially about the latter two topics in a single one-hour interview. However, there would seem to be no good reason for concealing information about their menstruation from a female social worker. This finding would therefore appear to be significant for the patients studied. It is of interest that a higher percentage claimed sexual satisfaction in the prolonged vomiting and toxaemia groups compared with the control and prolonged labour groups. This may well reflect a "covering up" of basic dissatisfaction about their sex life—it is not possible to state the meaning of this difference which did not however reach statistical significance.

In summary a signficantly higher incidence of stressful life situations was found in the complicated pregnancies. These patients also had a higher incidence of bodily symptoms prior to pregnancy. There was some evidence of rejection of pregnancy by patients with prolonged labour and toxaemia. These findings in addition to those already reported, provide some support for a psychosomatic hypothesis for these conditions (HALLIDAY, 1948; WOLFF, 1953; HETZEL, 1960). It is apparent that stressful life experiences during pregnancy are only one of a combination of possible factors in producing such abnormal states. Evidence of the importance of genetic factors as exemplified by body build has been presented by COPPEN (1958; 1959) while personality factors have been emphasised by CRAMOND (1954; 1956) in prolonged labour and also by COPPEN (1958; 1959). However, the effect of such stressful life situations may be prevented or lessened considerably by suitable measures—their recognition is therefore important for those in charge of such patients.

SUMMARY

A comparison has been made between the incidence of stressful life situations during primiparous pregnancy in 44 patients with prolonged labour, 30 patients with prolonged vomiting and 40 patients with toxaemia compared with 54 patients with

normal pregnancy and labour. A significantly higher incidence of interpersonal, economic and occupational problems was found in the patients with prolonged vomiting and toxaemia of pregnancy. There was some evidence of rejection of the pregnancy in patients with toxaemia and prolonged labour. An increased incidence of bodily symptoms prior to pregnancy was noted in all three groups of patients with complications.

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VOL.
5
1960/6

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SOME BEHAVIOURAL AND OTHER CORRELATES OF CHOLESTEROL METABOLISM*†

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INTRODUCTION

THE aetiology of coronary heart disease, and especially the role of cholesterol metabolism and atherosclerosis, has been widely studied.

Correlations have been made between plasma lipid levels and diet (KEYS, 1957; PAGE, 1957; BEVERIDGE, 1957; FRIEDMAN, 1958), age and sex (GERTLER, 1954), body-weight and build (TANNER, 1951; MJASSNIKOW, 1957). Physical activity (BENTON, 1954), heredity (SCHAEFER, 1958; RUSSEK, 1958), occupation, stress (HAMMARSTAN, 1957; SPRAGUE, 1958; BROWN, 1951; PEETE, 1955; FRIEDMAN, 1959) and personality (DUNBAR, 1943; STORMENT, 1951; MILES, 1954) have all been variously indicted. However, personality investigations, in particular, have been hampered by the fact that what have usually been studied are the end-states rather than the beginning processes of such disease. Thus, MILES *et al.* (1954) accepted as significant those differences found between their experimental and control groups which showed that the former were relatively less introspective and were capable of the freer expression of aggression. Their apparently greater tendencies towards tension, worry and general neuroticism, however, they dismissed as being simply reactions to the fact that these individuals had had attacks of coronary occlusion. The fact that these patients were also apparently less intelligent and sophisticated was attributed to the inadequate matching with the control group for socioeconomic class since the latter contained more persons of relatively higher status. Thus SPRAGUE (1958) quotes a passage from this study: "No one yet has demonstrated in humans that stresses of a magnitude compatible with a 'normal' life can influence the deposition of cholesterol material in the coronary vessel walls . . . We simply do not have evidence . . . that anxiety or other emotional stress is related to the genesis of atherosclerosis." as a refutation of the notion that psychological factors can play a role in the genesis of coronary artery disease. It might on the other hand be more proper to decide that no conclusions, either positive or negative, can in fact be drawn from this study because of the incorrect sampling method.

That the end processes of coronary artery disease may be influenced by the emotions is probably no longer controversial. Thus, it is known that the severity of anginal pain may be accentuated by the emotional state of the patient and acute coronary occlusion with myocardial infarction can be precipitated by severe emotional crisis (TANNER, 1951). The hypothesis that certain patterns of personality underlie the genesis of the disease is, however, much more debatable. Here one is upon much less secure ground and the majority of studies seem more marked by literary descriptive power than scientific accuracy.

Thus, Osler pointed to the fact that it was not the "delicate neurotic person who was prone to angina, but the robust, the vigorous in mind and body, the keen and ambitious man, the indicator of whose engine was always at full speed ahead."

DUNBAR (1943), whose detailed study may well have influenced many subsequent workers, described the coronary patient as having little interest in sports, and few hobbies, but as being an excessively strenuous worker who went many hours without vacation under stress and strain. He was prone to stick to one job for many years and marked by compulsive or depressive neurotic tendencies. His educational history showed a decided trend toward completion of whatever scholastic

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unit was undertaken and he presented surface calm with little appearance of the strain evidenced in patients with hypertensive cardiovascular disease. Both she and ARLOW (1945), who later reported psychiatric observations in 13 of these cases, stressed the psychodynamic importance of the patients' childhood conflicts with authority. ARLOW, in particular, described the early competitive relationship with the feared and envied parent who was usually the father. This led to the suggestion that the characteristic method of defence was repression and identification which failed because of the constant recreation of new forms of the original competitive situation.

GILDEA (1949), summarising views on sociability and acceptance, stressed the need and respect for authority of these patients and their unremitting compulsive compensatory work. Their planned careers led frequently to executive and managerial positions. However, such traits were contrasted with feelings of insecurity and inferiority.

Nevertheless, STORMENT (1951), using a more objective questionnaire method, was unable to confirm such suggestions in a small series of patients. GLATZEL (1951) stressed emotional directness and sympathy, and PEETE (1955) the conservativeness, impatience, anxiety, conscientiousness and driving qualities which led to long working hours, little recreation, poor sleep and immoderate dietary habits. He also linked paradoxical traits of aggression and mildness.

It has, then, been consistently suggested that there is in the behaviour of these patients a pattern of competitiveness which in itself does not lead to satisfaction, but rather results in compensatory activities which fail completely to resolve the underlying anxiety.

On the physical side, a mesomorphic or muscular body structure and high cholesterol levels seem to be frequent findings in patients with coronary disease. It is possible that these are genetically linked so that an intrinsic fault of cholesterol metabolism might prove to be the major component of lipid disturbance leading to atheroma formation and thus eventually to coronary occlusion.

This suggested to us that one way of studying such relationships might be to investigate the personality traits related to cholesterol. However, one of the difficulties well recognised in the criticisms which have been made of previous studies lay in the lability of the index of cholesterol metabolism, dependent as it is upon diet. Fortunately, an extensive research on the influence of diet on cholesterol at Queen's University enabled us to obtain a sufficient number of students who had been on a strictly controlled fat free diet. In this way, it was possible to avoid errors of the kind criticised by JOLLIFFE (1959) who has pointed out that the marked change of serum cholesterols due to socio-economic stress in accountants during the period of their deadlines occasioned by the taxation year, were merely a result of their different dietary intake at this time. Certainly, Sprague has suggested that it seems likely that emotional tension might compensatorily result in compulsive eating, drinking and smoking, which might secondarily influence coronary disease. However, the exclusion of dietary choice and extrinsic fat provided material for a more controlled study with cholesterol as an independent variable. It is recognised that, although the associated findings were dependent, the relationship was not necessarily one of cause and effect.

METHOD

A group of normal student volunteers who had an abnormally high fasting cholesterol level (i.e. greater than 165·5 mg per cent) after eight days of fat free diet were compared in the respects described below with another student group whose level under identical conditions was abnormally low (i.e. less than 107 mg per cent). There were 11 males and 2 females in the former group and 13 males in the latter. They were chosen from a group of 178 students, whose mean fasting cholesterol level was 137·5 mg per cent, as being either at least one standard deviation above or below this mean on the cholesterol index (see Fig. 1).

VOL.
5
1960/6

There was no significant difference between the criterion groups in either age or intelligence.

(1) *Medical history*

Individual medical histories were taken in which particular attention was paid to family history of coronary heart disease, hypercholesterolaemia, hyperthyroidism, renal disease, hypertension, psychosomatic or psychiatric problems, previous neurotic traits and physical health of the individual and evidence of social adjustment in life.

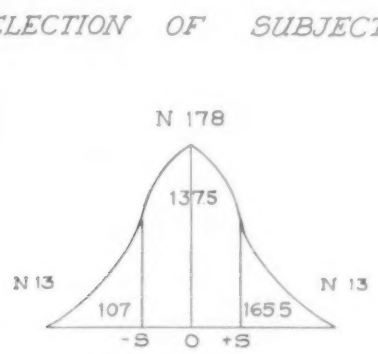

FIG. 1. Fasting cholesterol level mg per cent after 8 days of fat free diet.

(2) *Somatotyping*

Somatotyping was done by the phenotyping method of PARNELL (1958). His deviation chart is known as the M4 since it is based on the assumption that a rating of 4 in muscularity will bear a constant proportional relationship to stature. Components in the M4 chart are termed fat, muscularity and linearity, in place of Sheldon's endomorphy, mesomorphy and ectomorphy. Parnell's method is objective and consistent. It is simple and speedy and less subject to variable interpretations by different observers. The inter-observer error with the M4 chart depends only on the accuracy with which measurements are taken. The anthropometric measurements are height in inches, weight in pounds, bone measurements of humerus and femur in centimetres, muscle girth of biceps and calf and skinfold measurements of subcutaneous fat in centimetres over the subscapular, supra-iliac and triceps regions. In addition, to keep a permanent record of our subjects, the photographic technique developed by BROWN and MOTT (1951) at Queen's University was also used.

(3) *Psychiatric studies*

The psychiatrist involved in the study was unaware of the cholesterol levels of the students. Each subject was seen in an individual psychiatric interview which usually lasted for some hours. 17 subjects, 8 with low cholesterol indices and 9 with high, attended group meetings. These were run along the lines of group analytic discussions. An extra female volunteer was asked to attend the group without a girl to make the two group meetings more comparable. Ten weekly meetings of one and a half hours were conducted.

(4) *Sociometry*

A sociometric test of preference was carried out in each group at the end of 5 weeks of group meetings. Each individual was asked to state with whom amongst the members of his group he would like to work, play and eat.

(5) *Adjective rating scale*

Each subject was asked to rate himself and his "ideal self" on an adjective rating scale covering 18 dimensions of personality (BUSS and GERJUOY, 1957) divided into verbal hostility, physical hostility, hostile attitudes, physical sexuality, sexual attitudes, anxiety, mood, guilt, self-esteem, ideation, impulsiveness, guardedness, flexibility, emotional warmth, sociability, autonomy, dominance and ambition. Each dimension contained up to 20 adjectives descriptive of varying quantities of each trait: i.e. verbal hostility varied from "venomous" at one end to "eulogistic" at the other, through intervening quantities of hostility, such as "sarcastic", "outspoken" and "complimentary".

(6) *Personality tests*

Because the psychiatric and psychological research started concurrently, the original psychological investigations were entirely empirical. It was concluded that previous psychological research reported in the literature was so poorly controlled or so negative, that no reasonable hypothesis could be formulated. A large number of relatively independent personality tests were therefore used with the intention of testing as wide a range of personality characteristics as possible. Thus 64 items of the Cattell objective analytic battery were administered. In addition, however, the Cattell 16 PF personality tests and the Guilford Inventory STDCR were used not only to provide further broad coverage, but also to afford comparison with previous studies of coronary patients (STORMENT, 1951; MILES *et al.*, 1954).

RESULTS

(1) *Medical history*

The high cholesterol group had a higher incidence of family history of coronary heart disease, whereas the family of the low group seemed weighted with more miscellaneous illness, such as rheumatism, multiple sclerosis, asthma, hay fever and peptic ulcer. There were more personal major operations performed between the ages of 6 and 10 in the low group, such as tonsillectomy, appendicectomy, hernia, broken bones and a greater number of neurotic traits in childhood, enuresis, sleep-walking, nail-biting, stealing. Five out of 13 in the high group were the only children in the family. These findings were all significant on a Chi square test at the 3 per cent level of confidence.

(2) *Somatotyping*

Mesomorphy (muscularity) was positively correlated (+0·208) with high cholesterol whereas ectomorphy (linearity) and endomorphy (fatness) were negatively correlated (—0·250 and —0·212 respectively).

(3) *Psychiatric studies*

(i) *Individual interviews.* The high cholesterol subjects were aggressive and outgoing but self-critical. Their own strictures seemed to act as a spur to further endeavour.

VOL.
5
1960/6

The low cholesterol subjects were better satisfied with themselves, more easygoing and friendly. Self-depreciation was rare and seemed to lead to anxiety and fear of failure.

(ii) *Group sessions.* The low cholesterol group appeared to be more co-operative and sociable. They discussed a wider range of topics and the majority participated in the talk. They seemed more empathic with each other without marked competition for leadership. They were not argumentative and their attitude was flexible and friendly so that the observer therapist felt at ease and that his role was one more of

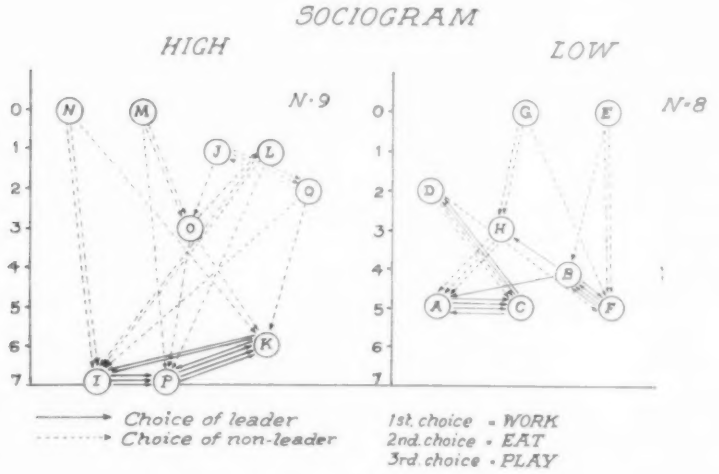

FIG. 2

catalytic encouragement. On the other hand, the high group seemed extraverted and verbally aggressive. They argued repetitively about similar matters. There was a considerable degree of competition for leadership and they were dominated by one subject who was outspoken and energetic. The observer therapist felt ill at ease so that his role seemed most frequently to be placatory.

(4) *Sociometry*

In the high cholesterol group there were 3 mutually chosen leaders, each leader choosing the other and also chosen by the individuals in the group. Thus, the 3 leaders formed a separate sub group. In the low group the 4 leaders, ACF and B, chose more the other members of the group, pointing to a degree of mutual interaction (see Fig. 2).

(5) *Adjective rating scale*

(i) *Rating of self.* The high cholesterol group showed consistently greater mean scores of physical and verbal hostility and hostile attitudes than the low group ($P < 0{\cdot}05$). The summated score of total hostility was also significantly greater (see Table 1).

(ii) *Rating of ideal self.* There was no difference between the two groups when their ratings of ideal self were compared.

(iii) *Comparison between the ratings of self and ideal self.* The subjects in the low group desired to be significantly less anxious (see Table 2).

The subjects in the high group wished to be less hostile, very much less anxious, but more sociable (see Table 3).

TABLE 1.—COMPARISON OF SELF RATINGS IN LOW GROUP AND HIGH GROUP

Self ratings	Group		t	P
	Low ($N = 13$) Mean score	High ($N = 13$) Mean score		
Verbal hostility	9·00	10·61	—	N.S.
Physical hostility	8·15	8·31	—	N.S.
Hostile attitudes	8·46	10·92	2·95	0·02
Total hostility	8·56	10·00	2·27	0·03

TABLE 2.—COMPARISON OF RATINGS OF SELF AND IDEAL SELF IN LOW GROUP

	Self	Ideal self	t	P
Anxiety	9·10	7·08	2·73	0·02

TABLE 3.—COMPARISON OF RATINGS OF SELF AND IDEAL SELF IN HIGH GROUP

	Self	Ideal self	t	P
Verbal hostility	10·61	8·08	2·40	0·03
Hostile attitudes	10·92	7·30	3·96	<0·001
Anxiety	9·54	7·08	4·24	<0·001
Sociability	7·15	9·90	3·50	0·004

(6) *Personality tests*

Of the 96 personality measures obtained, only one differentiated between the two group means at better than 5 per cent level of significance. This was expected by chance and it was concluded that there were no real mean differences between the two groups on these tests. On 8 of the 96 scores, one group was found to be more homogeneous than the other at the 5 per cent level or better using an F ratio although these were not associated with mean differences. There was, however, no consistent tendency for either the high or the low group to be the homogeneous group. These significant F ratios were associated with extremely non-normal statistical distributions. Thus, it was concluded that these differences were also likely to be chance findings because under these circumstances an F test is not strictly applicable.

DISCUSSION

It seemed from these findings that the group with high cholesterol met their needs mainly by aggressive competition, but at the same time feeling guilty and anxious, fearing that such traits alienated them from their fellows. The low group, on the other hand, had fewer overt conflicts, were better satisfied with themselves and perhaps more ready to accept dependency. It seemed probable, especially in view of the discrepancy

VOL. 5 1960/6

between self and ideal self ratings, that the high group were the abnormal subjects. They were certainly less satisfied with themselves although not necessarily manifestly anxious.

These distinguishing traits, although apparent in behaviour and subjective estimates, were not evinced in the results of the objective tests of personality. Such a finding was not entirely unexpected, as an empirical psychological study of this sort is unlikely to yield positive results in view of the very large number of personality characteristics it is possible to measure objectively. If, later, it is proven that personality patterns related to hypercholesterolaemia are also related to coronary heart disease, these negative psychological test findings might lend some weight to the interpretation of MILES *et al.* that some of their observed differences were reactive to the illness itself and also confirm STORMENT's results.

Nevertheless, these preliminary findings suggested that an intrinsic defect of lipid metabolism was linked to certain personality traits which in turn might lead to unsatisfactory life situations. The resultant emotional conflicts might well have cardio-dynamic accompaniments mediated by the catecholamines. These if constantly invoked in the presence of other predisposing factors (of which a high lipid level is probably an important one) could provide the substrate of later coronary disease. Thus, dietetic habits whether culturally or emotionally determined might assume lesser importance in the genesis of coronary heart disease than has been suggested by some.

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VOL
5
1960/

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STRESS INDUCED STOMACH LESION AS RELATED TO DESTRUCTION OF THE SYMPATHETIC GANGLIA*†‡

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THE results of a series of studies (SINES, 1959, 1960, 1961) of a substrain of rats which are susceptible to stress induced gastric ulcers have led to the hypothesis that the ulcer susceptible animals show parasympathetic dominance or are functionally sympathectomized. Since the literature dealing with the effects of surgical interruption of the sympathetic innervation of the stomach is equivocal a non-surgical procedure for the reduction of sympathetic innervation was sought.

COHEN (1960) and LEVI-MONTALCINI and BOOKER (1960) have reported an antiserum to a nerve growth protein which does in fact markedly and selectively reduce the number of cells in the sympathetic chain ganglia of newborn rats and other mammals. In their studies, LEVI-MONTALCINI and her associates have found that following repeated injections of the antiserum in newborn rats the number of cells found in the superior cervical ganglia is reduced to less than 10 per cent of the number normally found in control animals.

The following report deals with behavioural study and incidence of stress induced stomach lesions in the rat following partial destruction of the sympathetic ganglia by means of Levi-Montalcini's nerve growth protein antiserum.**

METHODS AND MATERIALS

Four groups of 10 male Sprague-Dawley rats each were studied. Animals in the Experimental Group received 0·3 ml of the antiserum on each of 2 consecutive days beginning within 2 days of their birth, at which time their tails were clipped for identification purposes. Animals in Control Group 1, litter-mates of the Experimental animals whenever possible, received no injections nor were their tails clipped. A third group of 10 animals had their tails clipped within the first 2 days following their birth, while the fourth group received 0·3 ml of physiological saline on each of 2 consecutive days, beginning within 2 days of their birth. Injections were administered subcutaneously high on the animal's back.

All animals were weaned at 21 days of age and group housed by litters. There were from 3 to 5 animals in a cage where they lived until the experiment was terminated. *Ad lib.* food and water were available at all times. Animals were weighed at 2-week intervals and the last weighing was done when the animals were 84, 85, or 86 days of age.

After the last weighing animals were placed individually into a 3 × 5 foot open field and observed for a 2-min period. The floor of the field was marked off into 1 ft squares and was surrounded by a galvanized metal wall 24 in. high. The three aspects of the animals' behaviour which were noted were the number of squares entered, the number of times an animal reared on its hind legs and the number of fecal boluses deposited in the field during the 2-min period.

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† This study was conducted by the senior author in partial fulfillment of the requirements for the MA degree under the direction of the junior author.

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Approximately 30 min after the open field test the animals were immobilized individually in confining wire mesh cocoons for 12 hr during which period neither food nor water were available to the animals.

After 12 hr of immobilization the animals were removed from the cocoons and sacrificed with ether. The stomachs were removed and examined independently by two observers who rated them on a 0 to 4 point scale. On this scale, zero indicated a normal stomach; "1" small petechiae; "2" irregularity of the mucosal lining; "3" a clearly defined defect which usually involved bleeding; and "4" the most severe lesion observed, being a palpable defect which almost invariably included considerable congealed blood in the base of the crater.

TABLE 1.—EFFECT OF ANTISERUM INJECTION ON THE NUMBER OF CELLS OF THE SUPERIOR CERVICAL GANGLIA AND LESION SEVERITY

Animal	Number of cells experimental	Destruction of Sup. Cerv. Gang. (per cent)	Lesion severity
1	5599	92	4
2	6251	91	4
3	44 478	37	3
4	73 079	0	1
5	45 002	36	2
6	52 905	25	0
7	49 561	29	0
8	31 479	55	1
9	28 279	60	2
10	18 984	73	2

The dead animals were decapitated and the heads placed in a 70% alcohol solution for 1–2 hr, at which time the superior cervical sympathetic ganglia were dissected out and examined histologically to determine the number of cells present.

RESULTS

There were no reliable differences between any of the groups in any of the open field measures or in body weight.

The cell counts for each experimental animal are presented in Table 1. On the basis of cell counts of the superior cervical ganglia in three animals from Control Group 1, 70,000 cells was considered to be the normal figure. The percentage reduction in the number of cells in the ganglia of each of the animals injected with the antiserum are also presented in Table 1.

It can be seen that the reduction in number of cells in the cervical ganglia was far from uniform or complete. This irregularity was attributed to variability in the potency between the several batches of antiserum employed, an interpretation which was corroborated independently by investigators in Levi-Montalcini's laboratory using some of the same batches of antiserum in other studies. In spite of the great variability in the amount of reduction in the number of ganglion cells, there remained a marked difference in both size and cell numbers between normal and injected animals.

The data relating to the number and severity of stomach lesion in each of the groups are summarized in Table 2. The Experimental Group showed a higher incidence of lesions with ratings of 2, 3, and 4 (indicating greater severity) than did any of the other groups, although one of the differences failed to reach an acceptable

VOL. 5 1960/6

level of significance. The significance levels of the comparisons are presented also in Table 2.

One further comparison involved the rank order correlation between the percent reduction in number of cervical ganglion cells and stomach lesion severity in the experimental group. The obtained rho was +0·77 with a probable error of 0·09, indicating a clearly significant relationship between the loss of cervical ganglion cells and severity of stomach lesion which followed stress.

TABLE 2.—STOMACH LESION INCIDENCE IN THE EXPERIMENTAL AND CONTROL GROUPS

Group	*N*	Percent with lesions rated 2, 3 or 4	Significance of comparison with experimental group
Experimental	10	60	
C 1	9	33	<0·03
C 2	9	44	<0·15
C 3	9	11	<0·01

DISCUSSION AND CONCLUSIONS

The data presented here indicate that moderate to marked reduction in the number of cells in the cervical ganglia is related to a higher incidence of stomach lesion development in the rat under stress. These data further suggest that the degree of loss of cervical ganglion cells in the rat is related to the severity of stomach lesions which follow 12 hr of immobilization.

These results are interpreted as further support for the notion that parasympathetic dominance is involved in the susceptibility of the rat to immobilization induced stomach lesions.

The lack of any significant difference in weight or in open field behaviour failed to support our expectations regarding those variables. Further the lack of differences in weight and behaviour suggests that the effects of reduction in the number of cells in the sympathetic ganglia may be restricted in range and do not involve function under relatively non-stressful conditions. Thus, where *ad lib.* food and water were available those animals with partially reduced sympathetic ganglia may have been under no handicap. It seems reasonable to expect, however, that under less benevolent conditions the survival value of the intact sympathetic system may have been manifest by both weight and behavioural differences.

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A SYSTEMATIC STUDY OF AUTONOMIC DRUG ACTIONS IN MENTAL HOSPITAL PATIENTS: METHODOLOGY AND PRELIMINARY RESULTS*

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MANY drug studies aimed at testing the autonomic reactivity of mental patients have been carried out more or less systematically over the past 50 years (PÖTZL *et al.*, 1910; MYERSON *et al.*, 1937; FUNKENSTEIN *et al.*, 1950; HOFFER, 1954, for a survey see CYVIN *et al.*, 1956). Methacholine, usually in conjunction with epinephrine, has been widely used for this purpose in more recent years, and the consequent physiological (MYERSON *et al.*, 1937) and psychological (LINDEMANN and FINESINGER, 1938) responses have been taken as criteria of individual autonomic balance and reactivity. Generally, rapid intravenous injection of epinephrine (25 or 50 μg) and intramuscular injection of metacholine (10 mg) are used (FUNKENSTEIN *et al.*, 1952*a*), and the dosage levels are standardized without regard to body weight. Few attempts have been made to improve this technique (CYVIN *et al.*, 1956).

Even though the response to epinephrine *per se* has appeared to be of no value in differentiating between individuals (FUNKENSTEIN *et al.*, 1952*a*), the blood pressure effects of both epinephrine and metacholine have usually been taken together to establish a response pattern presumably separating subjects into various groups. Heart rate changes do not seem to have been considered and they are usually not mentioned. Subject age has also not been considered in clinical experiments despite evidence of its importance (NELSON and GELLHORN, 1957). The separation of patients into different groups on the basis of blood pressure reaction patterns has been statistically correlated with such rather complex factors as psychiatric diagnosis and the outcome of E.C.T. and other therapies.

Although initially results were described as very promising and were widely accepted and reproduced (BROTHERS and BENNETT, 1954; ALEXANDER, 1955; JONES, 1956; SLOANE *et al.*, 1957; RAMAPURAM, 1958), more recent work has led to considerable doubt as to the objectivity and reliability of this testing procedure (CYVIN *et al.*, 1956; CLEMENS, 1957; LOTSOF and YOBST, 1957; GROSZ and MILLER, 1958; MAAS, 1958). As results have been more critically interpreted, more limited conclusions have been made (SLOANE *et al.*, 1958; LUNDE *et al.*, 1958), and the most recent reports on this subject have been negative (HOFFER and CALLBECK, 1959*a*; SATTERFIELD, 1959; OZTURK *et al.*, 1959; BRAWN and RETTEK, 1959) with but few exceptions (KAMP and BERGHORST, 1959).

Another drug which has been in some use in testing is atropine (HOFFER, 1954; DOUGLAS and HOCH, 1956). Here again blood pressure response has been used for correlation with diagnosis, but the test is not claimed by its originator to be helpful for clinical purposes (HOFFER and CALLBECK, 1959*b*). Attempts have been made by

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VOL.
5
1960/6

others to use the amount of atropine needed to produce orthostatic phenomena as a criterion for the separation of individuals into reaction groups (DANIELOPOLU and CARNIOL, 1923; FISCHER *et al.*, 1959). Atropine as a test drug does not seem to have evoked much interest, and is still awaiting a critical evaluation.

In addition to autonomic drugs, sedatives have also been used for similar test purposes (SHAGASS, 1954). The amount of intravenously infused barbiturate required to sedate the patient (the sedation threshold) has been claimed to correlate with anxiety and tension in neurotic subjects, and to differentiate between neurotic and psychotic depression, thereby indicating appropriate treatment (SHAGASS and NAIMAN, 1956; SHAGASS and JONES, 1958). Difficulties have, however, been encountered in accurately determining this "sedation point", using the suggested end points of the slurring of speech and the increase in 15–30 cycle/sec waves in frontal E.E.G. leads (THORPE and BAKER, 1957; BRADLEY and JEAVONS, 1957); and the initial procedure was later modified into the sleep threshold test (SHAGASS and KERENYI, 1958; SHAGASS *et al.*, 1959). But in a recent very careful study neither test modification appeared to be significantly correlated either with the degree of anxiety or with diagnostic groupings (ACKNER and PAMPIGLIONI, 1959).

Thus, the development of the clinical application of autonomic drug tests would not appear very promising for the future. Neurophysiological experiments, however, corroborate the idea that the effects of autonomic drugs can be changed by alterations in hypothalamic reactivity, whether this be induced by hypothalamic lesions or by injections of depressant drugs into the hypothalamus (GELLHORN, 1957). On the basis of these experiments, norepinephrine was considered to be a more suitable test drug than epinephrine.

Psychological "stress" experiments of the most varying types have been extensively used to clarify the connection between affect and autonomic changes (FUNKENSTEIN *et al.*, 1957; AX, 1955). Excretion patterns of epinephrine and norepinephrine have been studied (FUNKENSTEIN *et al.*, 1952*b*; ELMADJIAN *et al.*, 1957; BERGSMAN *et al.*, 1959), and appear to be contributing to the understanding of the nature of psychotic and neurotic states of excitation. Apparently the subject of autonomic changes connected with mental disturbances is of imperishable interest to psychiatrists and to allied psychologists, physiologists and, lately, to biochemists as well.

The present study was undertaken as a part of a research project designed to elucidate variations in clinical, psychological, sociological, biochemical, pharmacological, and physiological patterns within a varied group of hospitalized schizophrenic patients and to compare these with a similarly hospitalized group of non-schizophrenic patients (GERARD, 1960). The results of experiments with yohimbine as a test drug have been previously reported (HOLMBERG and GERSHON, 1961). The present paper is a description of the methodology established after a year's experimentation with various autonomic drugs, and of the results obtained in some 200 drug testings.

METHODS

Two preliminary recording sessions proceeded all drug experiments. The first session was an acclimatization session to familiarize the patient with the procedure. The second session was used to obtain a baseline recording in a relaxed state. All possible care was taken to handle the patients so as to induce as little fear and anxiety as possible by the recording situation itself. The climatic surroundings were kept, as far as possible, pleasant and constant with the help of air-conditioning and humidifying devices.

Drugs were intravenously injected at a slow, even rate, and dosage was adjusted to body weight. A few minutes before the experiment a heparinized permanent cannula was inserted into the vein and drugs were later administered through a rubber membrane on this cannula. In this manner it was possible to avoid the pain and the loss of time involved with repeated venipuncture. Each experimental period began with a 5 min period of baseline recording, immediately followed by drug application. The delayed drug action and recovery were continuously recorded after the injection period.

A systematic recording of the effects of preparatory procedures was carried out before yohimbine and norepinephrine tests. In these studies the baseline recording was followed by a 2 min period to allow for insertion of the needle, another 2 min period during which normal saline was injected, and a final 1 min period for recovery before the drug injection. In two cases two drugs were given in the same experimental session, with an interval of 30 min, *viz.* norepinephrine + methacholine and epinephrine + atropine.

The norepinephrine and methacholine experiments, the yohimbine experiment, and the psychological stress experiments were carried out in the polygraphic section of the laboratory using Model T Offner E.E.G. as a recording instrument. The recordings so far analyzed consist of an E.K.G. (to determine heart rate) and an automatic systolic blood pressure recording.* Because of difficulties with the latter, some data on blood pressure effects are lacking. The other experiments were done in the E.E.G. section, a Grass E.E.G. being used for recording of the E.K.G., and blood pressure measured by auscultation every 30 sec. In all cases, timing of the experiments was rigorous and the injection of each volume unit was marked on the record by means of a foot-operated electrical signal.

The dosage levels of the various drugs were as follows:

Sodium Pentothal (for sleep threshold) 0·75 mg per kg/min, for a maximum of 10 min.
Megimide (for subconvulsive threshold) 0·3 mg/kg/min, for a maximum of 10 min.
Epinephrine 0·2 μg per kg/min, administered over 6 min.
Norepinephrine 0·25 μg per kg/min, over 6 min.
Methacholine 5 μg/kg/min, over 6 min.
Atropine 2 μg/kg/min, over 5 min.
Piperoxan 0·05 mg/kg/min, over 5 min.
Yohimbine hydrochloride 0·1 mg/kg/min, over 5 min.
All subjects weighing over 80 kg were given a dosage calculated to 80 kg.

A 6 min injection period was employed with the quickly-acting drugs because the first minute was needed for adjustment to a more steady level and could thus be disregarded, while the state during the last 5 min of injection formed a good basis for comparison with the baseline before injection. Atropine, piperoxan and yohimbine had more slow and long-lasting effects which had to be followed for at least 15 min after the injection.

The sleep threshold determination was carried out as follows: E.E.G. was recorded from six different frontal leads. During the injection of Pentothal the patient was asked to tap on a switch continuously, and each tapping was recorded along with the E.E.G. and the injection markings. When the tapping eventually stopped the patient was told to continue tapping, and injection was continued until there was no reaction to this urging. The amount of drug injected up to this point was taken as a measure of the sleep threshold. The patient was still regularly told to continue tapping. From 1 to 10 min was usually required before tapping was resumed, and this period gave a fair estimate of the duration of sleep. The E.E.G. findings were found so difficult to quantify that the cessation of tapping had to be used as the only criterion for sleep threshold. This, however, seemed to provide an accurate measure and all patients cooperated very well under the influence of the drug.

The "subconvulsive threshold", as we prefer to call it because convulsions were avoided as far as possible, was determined in the following manner: Eight frontotemporal, temporal and temporoparietal E.E.G. leads from ten electrodes were used. The E.E.G. was continuously observed during the injection of Megimide, and injection was terminated when any of the following signs appeared: (1) A clinical seizure: (2) Myoclonic jerks in connection with spikes in the E.E.G.; (3) Repeated large spikes (over 150 μv); (4) Spike-wave episodes lasting more than a couple of seconds or rapidly repeating; (5) Loss of consciousness, extreme discomfort, or undue effects of any kind. The termination of injection and the reasons for it were marked on the record. In some cases the complete dosage of the drug (3 mg/kg) could be given without any such signs appearing, but there were some

* "Continuous Systolic Monitor", manufactured by Biophysical Electronics, Inc., Great Neck, New York.

VOL. 5 1960/6

E.E.G. signs even in these cases which enabled us to rank all patients according to the rapidity of their appearance during the injection period.

The order of appearance of E.E.G. phenomena was: (1) Theta (4–7 cycle/sec) waves of over 25 μV amplitude; (2) Theta waves of over 50 μV amplitude, generally in the form of bursts; (3) Theta waves of over 75 μV amplitude, soon followed by delta (1–3 cycle/sec) waves of the same amplitude; (4) Repeating "microspikes" or 5–6 cycle/sec spike-wave bursts; (5) Spikes over 100 μV amplitude and/or 3–4 cycle/sec spike-wave or similar activity; (6) Generalized large spikes (over 150 μV), sometimes connected with myoclonic jerks; (7) Frequent large spikes or enduring delta activity, which were signs of an imminent grand mal attack. Two minutes after cessation of megimide injection, sodium amytal (0·5 g) was slowly injected. Upon returning to the ward the patients were also given 0·1 g phenobarbital orally in order to prevent late seizures. The discomfort created by the convulsant drug was also promptly abolished by the sedatives.

The first psychological stress experiment consisted of blindfolding the patient, attaching earphones without his knowledge, and playing a stereophonic high-fidelity tape-recording of voices and noises from the laboratory milieu over a 5-min period. The content of the tape-recording dramatically indicated that the patient's reactions were unduly intense, that the experiment was going badly, conflicting comments concerning the patient were made, etc. In most cases the patients did not realize that the dramatic scene was recorded, but several of them did think it was "put on" directly by the laboratory personnel.

The other stress procedure consisted of painful shocks given automatically every 15 sec over a period of 5 min. The patient could postpone a painful shock for a full 15 sec by pressing a button at any time and thereby giving himself a small shock. The inner conflict arising from the choice between the two kinds of unpleasant experience and the growing uncertainty of timing and need for action as the strong shock becomes imminent was intended to create a state of tension and anxiety in the patients.

The degree of emotional reactivity exhibited by the patients was independently rated by seven raters, four of whom were psychologists, one a psychiatrist, one a well-trained nurse and one a ward attendant. All raters had observedthe patients over a 2 month period, three of them in psychological test situations, two in the milieu of the psychophysiological laboratory (the authors), and two during daily life on the ward. The rating was done on a bipolar scale with eight well-described points, ranging from very unreactive state—0—over average reactivity—3—to strong over-reactivity (such that the patient could barely be handled in experiments)—7. Every rater was carefully instructed about the use of the scale and told to recall all noticeable reactions in the patients on occasions of stress such as testing, drawing of blood samples, social conflicts, etc. After giving each patient a score the rater was instructed to carefully rank the patients according to their emotional reactivity.

The statistical method used in this preliminary study, the Spearman rank order correlation (KENDALL, 1948), was selected because of its suitability for manual calculation. The method is reliable when the distribution of data is fairly even, and this criterion appeared to be met in the present study. The result of each experiment was correlated with the result of every other experiment and with three additional factors: Chronological age (years), the time spent in a mental hospital (months), and the mean rank of emotional reactivity.

MATERIAL

Twenty-one cases were studied. All were mental hospital patients, 13 having been classified as schizophrenics and 8 as non-schizophrenics by three independent psychiatrists. Three of the schizophrenics were of paranoic subtype and the remainder were more or less chronic, undifferentiated cases. Four of the non-schizophrenic subjects were subclassified as psychopathic disorders (one with a possible birth trauma), three as alcoholics (one of them rather severely brain-damaged after *delirium tremens*), and one as a syphilitic chronic brain syndrome. In some of the experiments (psychological stress, norepinephrine, methacholine, yohimbine, sleep threshold, and subconvulsive threshold) almost all these patients could be used. However, one patient had to be transferred because of increasing unrest and one eventually refused to continue with tests. Only 9 of the patients were available for the experiments with epinephrine

and atropine, and for the experiments with piperoxan only 9 of the remaining patients could be used.

RESULTS

Emotional reactivity rating

The efficiency of the rating of emotional reactivity was shown by the fact that the ranking list obtained from each rater correlated well with that of every other rater. KENDALL's Coefficient of Concordance (1948) was 0·711, which corresponds to $\chi^2 = 99{\cdot}5$ and a P value far lower than 0·001. The distribution of the cases over the reactivity scale deserves some analysis. Of the schizophrenic patients 9 were rated as having low emotional reactivity and 4 as having higher reactivity than the normal average, while 3 of the non-schizophrenic patients were of low reactivity and 5 of more than average reactivity. The mean scores for the schizophrenic patients ranged between 0·7 and 6·6 (mean 2·72) and for the non-schizophrenic patients between 1·3 and 4·8 (mean 3·25). Thus the distribution was on the whole similar for the two groups, the main difference being the wider range of emotional reactivity among the schizophrenics. Indeed, the 2 most over-reactive as well as the two most under-reactive cases were schizophrenics. The 2 most over-reactive ones were paranoics with a high degree of dysphoria, and both were very difficult to manage in an experimental setting. The 2 most under-reactive ones were semistuporous, very deteriorated, chronic cases with almost no visible reactions to any experimental manipulation. It is interesting to note that the one nonschizophrenic patient with a reactivity far below normal had a chronic brain syndrome following central nervous system syphilis. The next lowest score was held by the one alcoholic patient with severe brain damage after *delirium tremens*. The third subreactive non-schizophrenic was also an alcoholic showing early sign of deterioration.

TABLE 1.—CORRELATIONS BETWEEN EMOTIONAL REACTIVITY (MEAN RANKING LIST) AND SOME OTHER FACTORS (ALL 21 CASES).

Factor	r_s	P
Age	−0·519	<0·02
Time spent in hospital	−0·472	<0·05
I.Q. (Wechsler-Bellevue)	0·612	<0·01
Reaction time	−0·377	<0·1
Reaction time variability	−0·445	<0·05

From this distribution pattern it seems clear that no differences in autonomic reactivity could be expected between diagnostic groups, in so far as autonomic reactivity has any connection with emotional reactivity. Only by using the emotional reactivity rating as a parameter could correlations with autonomic drug effects be shown to exist. In Table 1 are shown the correlations between emotional reactivity and a number of other factors. Neither ceruloplasmin level (Abood), urinary potassium and sodium, blood and urinary creatinine, nor urinary potassium/creatinine ratio correlated significantly with emotional reactivity (r_s below 0·200).

DRUG EFFECTS

All the following factors were intercorrelated: (1) Emotional reactivity rating; (2) Age; (3) Time spent in hospital; (4) Baseline study; (5) Sleep threshold; (6)

VOL.
5
1960/6

Subconvulsive threshold; (7) Auditory stress; (8) Electric (skin) stress; (9) Yohimbine test; (10) Norepinephrine test; (11) Methacholine test; (12) Epinephrine test; (13) Atropine test; (14) Piperoxan test. Those correlations with a significance level of 10 per cent or greater are shown in Table 2. The remaining, insignificant correlations need not be presented in this preliminary paper.

The sleep threshold was found not to be significantly correlated with emotional reactivity ($r_s = 0{\cdot}374$), but correlations at the 10 per cent level of significance were found between sleep threshold and four of the autonomic drug effects. The subconvulsive threshold also lacked a significant correlation with emotional reactivity ($r_s = -0{\cdot}275$) and the correlation between sleep threshold and subconvulsive threshold was quite insignificant ($r_s = 0{\cdot}030$). There were fair to good correlations between subconvulsive threshold and age and baseline blood pressure.

None of the stress tests correlated significantly with emotional reactivity, but the two different stress tests intercorrelated fairly well. There were correlations also between these stress tests and some drug tests.

The heart rate increase with yohimbine correlated to the 1 per cent level of significance with emotional reactivity, while the blood pressure change did not bear any such correlation. It correlated, on the other hand, highly with the blood pressure effect of preparations for test. There was a fair correlation between the blood pressure effects of yohimbine and atropine.

The blood pressure increase with norepinephrine showed a fair correlation with emotional reactivity. Generally the norepinephrine reactions correlated well with baseline conditions. Between baseline blood pressure level and the blood pressure effect of norepinephrine there was a very good correlation. Heart rate effect of norepinephrine correlated negatively with heart rate effect of epinephrine. With lower age there was a more intensive blood pressure effect of norepinephrine.

The methacholine test produced rather scarce results, the only fair correlation being that between heart rate before the test and the increment in heart rate after methacholine.

Both heart rate and blood pressure changes in response to epinephrine showed high correlations with emotional reactivity although, because of the small number of cases, the significance was only at the 10 per cent level. Heart rate changes induced by epinephrine and nor-epinephrine were (negatively) intercorrelated at the 5 per cent level. There were several high correlations also with other test results, but because of the small number of cases these were not statistically significant.

Generally, subjects with pathologically low emotional reactivity showed a low heart rate response to epinephrine while the blood pressure reaction tended to be high. Sometimes the systolic blood pressure would exceed 200 mm Hg in such cases, while the average maximum was 150–160 mm. In sharp contrast to the normal reaction, the heart rate of these subjects only briefly accelerated and then decreased again, sometimes far below baseline level. This inverse heart rate reaction did not directly correlate with the blood pressure increase. A smaller dose of epinephrine, causing only a moderate blood pressure increase, still reduced the heart rate; which indicates that the slowing of heart rate is not merely a reflection of the blood pressure increase. Pretreatment with atropine (3 mg) or with dihydroergotamine (0·5 mg) did not tend to reverse this inverse heart rate response. Pretreatment with yohimbine (which has central stimulant effects) however, resulted in a change to the normal, positive, type of

TABLE 2.—RANK ORDER CORRELATIONS (r_s) AND SIGNIFICANCE LEVELS (P). ONLY CORRELATIONS WITH A P LEVEL NOT OVER 0·1 HAVE BEEN LISTED. HR = HEART RATE. BP = BLOOD PRESSURE

Test	Correlation with	N	r_s	P
Sleep threshold	Nor-epinephrine, BP change	13	−0·478	<0·1
	Methacholine, BP change	16	−0·440	<0·1
	Epinephrine, HR change	9	0·717	<0·1
	Epinephrine, BP change	9	−0·654	<0·1
Subconvulsive threshold	Age	19	0·541	<0·02
	Baseline study, BP	19	0·558	<0·02
	Shock stress, BP change	16	0·426	<0·1
Auditory stress HR change	Shock stress, HR change	18	0·549	<0·02
Auditory stress BP change	Shock stress, BP change	17	0·600	<0·02
	Nor-epinephrine, HR change	18	−0·544	<0·02
	Epinephrine, HR change	9	0·733	<0·1
Shock stress HR change	Auditory stress, HR change	18	0·549	<0·02
Shock stress BP change	Time spent in hospital	17	0·517	<0·05
	Subconvulsive threshold	16	−0·426	<0·1
	Auditory stress, BP change	17	0·600	<0·02
Yohimbine test HR change	Emotional reactivity	20	0·605	<0·01
	Epinephrine, HR change	9	0·667	<0·1
Yohimbine test BP change	BP change during preparations for test	20	0·697	<0·001
	Atropine, BP change	9	−0·800	<0·05
	Piperoxan, HR change	9	−0·713	<0·1
Norepinephrine test HR change (Decrease)	Baseline study, HR	21	0·474	<0·05
	Auditory stress, BP change	18	−0·544	<0·02
	HR baseline before the test	21	0·406	<0·1
	Epinephrine, HR change	9	−0·800	<0·05
Norepinephrine test BP change	Emotional reactivity	14	0·538	<0·05
	Age	14	−0·627	<0·02
	Time spent in hospital	14	−0·476	<0·1
	Baseline study, HR	14	−0·578	<0·05
	Baseline study, BP	14	−0·780	<0·001
	Sleep threshold	13	−0·478	<0·1
	BP baseline before the test	14	−0·538	<0·05
Methacholine test HR change	HR baseline before the test	21	0·461	<0·05
	Piperoxan, BP change	9	−0·633	<0·1
Methacholine test BP change (decrease)	(Sleep threshold)	16	−0·440	<0·1

VOL. 5 1960/6

TABLE 2 (*continued*)

Test	Correlation with	N	r_s	P
Epinephrine test HR change	Emotional reactivity	9	0·733	<0·1
	Baseline study HR	9	−0·750	<0·1
	Sleep threshold	9	0·717	<0·1
	Auditory stress, BP change	9	0·733	<0·1
	Yohimbine, HR change	9	0·667	<0·1
	Norepinephrine, HR change	9	−0·800	<0·05
Epinephrine test BP change	Emotional reactivity	9	−0·738	<0·1
	Sleep threshold	9	−0·654	<0·1
	Atropine, HR change	9	−0·621	<0·1
Atropine test HR change	Emotional reactivity	9	−0·683	<0·1
	Sleep threshold	9	−0·683	<0·1
	Epinephrine, BP change	9	0·621	<0·1
Atropine test BP change	Age	9	0·667	<0·1
	Yohimbine, BP change	9	0·800	<0·05
Piperoxan test HR change	Yohimbine, BP change	9	−0·713	<0·1
Piperoxan test BP change	Emotional reactivity	9	−0·850	<0·05
	Methacholine, BP change	9	−0·633	<0·1

heart rate response and at the same time the blood pressure increase was reduced to a more normal range.

The atropine effect on blood pressure correlated (negatively) at the 5 per cent level of significance with the blood pressure effect of yohimbine. The atropine effect on heart rate had a high correlation coefficient with emotional reactivity although again, perhaps because of the small number of cases, the significance was only at the 10 per cent level. As seen in Table 2 there were a few more correlations at this level for the atropine experiment.

The blood pressure increase after piperoxan correlated negatively at the 5 per cent level of significance with emotional reactivity, and also two correlations at the 10 per cent level were found between piperoxan effects and effects of other drugs.

DISCUSSION

We feel that the general technique of drug administration employed fulfills, on the whole, the needs of reliability and validity. The stability of environment, both on the ward and in the laboratory, seem to have been adequate. The patients were familiar with the experiments and did not react emotionally to the drug tests to any significant degree. This is shown by the fact that none of the baseline recordings before tests had any significant correlation with the rated degree of emotional reactivity. The insertion of an intravenous cannula followed by injection of saline generally caused a brief autonomic stimulation which, however, was found to subside in a few minutes so that the autonomic functions were stabilized when the test procedure was

started. Rigorous timing of the procedures and accurate dosage levels were considered essential and resulted in standard type responses which could be described in quantitative terms. The adjustment of dosage to body weight was found to be adequate, as none of the drug reactions correlated significantly with body weight.

The rating procedure for estimation of the degree of emotional reactivity was shown to have very high concordance among the raters. The concordance was found to exist also between raters who had observed the cases in quite different settings, two of them on the ward, three in psychological testing situations, and two in the psychophysiological laboratory.

The psychological stress experiments were included in the battery in an attempt to obtain more data of a "clinical" nature with which to correlate the drug experiments. It is difficult to say if the design of these experiments was suitable for the purpose. There are endless varieties of such "stress" experiments, the value of which is very much disputed. It would probably not be difficult to get strong enough stress procedures, but to produce a considerable psychic stress in mentally ill patients without touching the borders of dubious ethics is certainly not easy. Furthermore, it seems difficult to construct a psychological stress test which is equally meaningful as a stress to most varied individuals. Admittedly, this part of the study was more tentatively applied than the rest.

The attempt at using an automatic blood pressure recorder was largely a failure, and in the future only the auscultatory, manual method will be used. Intra-arterial blood pressure recording (CYVIN *et al.*, 1956) would be desirable but has its risks and is too disagreeable for the patients to be used routinely.

Because of the limited case material so far investigated, it seems too early to draw any more detailed conclusions from the results obtained, but some general trends deserve discussion. They will be checked when the full subject roster has been completed.

The emotional reactivity rating in itself ordered the patient material in such a fashion that it became apparent that attempts at demonstrating differences between diagnostic groups would be unsuccessful. We feel that a suitable rating procedure is needed to make studies of physiological (and perhaps also biochemical) patterns in schizophrenic patients more meaningful. We do not claim, of course, that our present rating of emotional reactivity is more than a crude first attempt at estimating the degree of preservation, exaggeration, or deterioration of the normally existing emotional functions. A refinement of the rating procedure can probably be arrived at, but we consider it essential that the total concept of emotional reactivity does not get lost in an attempt at bringing in detailed judgments.

The emotional reactivity, as rated, showed several correlations with other data which corroborate its meaningfulness. The correlation with I.Q. and reaction time experiments is an indication that in mentally ill individuals the intellectual and the emotional losses are bound to go together. The correlation with age and length of stay in the hospital is in keeping with the fact that a longer-lasting mental process leads to increasing deterioration of emotional functions. The lack of correlations with biochemical data may indicate only that the choice of biochemical tests was not meaningful in this connection. Probably studies of catechol amines and steroid compounds would give more information, and such studies are being included in this project.

VOL.
5
1960/6

The lack of a significant correlation between sleep threshold and emotional reactivity is in keeping with ACKNER's (1959) results in a similar and larger study. As a matter of fact most autonomic drugs gave better correlations with emotional reactivity than did the sleep threshold. Similarly, subconvulsive threshold did not give any sign of being useful for this purpose. It might have been expected that a convulsant and an anticonvulsant sedative drug would give negatively correlated results, but in actuality no correlation could be found.

Yohimbine has been more thoroughly studied in this project than the other autonomic test substances employed. In three different groups of cases the same good correlation has been obtained between heart rate effect and emotional reactivity (HOLMBERG and GERSHON, 1961). We thus feel certain that the finding is not coincidental. It seems reasonable that a drug which has central stimulant properties and which produces, as we have found, an anxiety-like state with accompanying autonomic symptoms, would also have a greater effect on individuals who are clinically found to have more excitable emotional and autonomic functions.

Piperoxan has similar properties in this respect although it is chemically unrelated. Piperoxan mainly produced a blood pressure increase, and the degree of this increase correlated negatively with the emotional reactivity. It also correlated negatively with the effect of yohimbine on heart rate, which further connects the two drugs. Quite in line with these findings, the heart rate response to epinephrine correlated positively, and the blood pressure effect negatively, with emotional reactivity. Furthermore the heart rate effects of yohimbine and of epinephrine were positively correlated.

The connection between these three drug effects is interesting because, although both yohimbine and piperoxan are know as adrenolytic compounds, the changes recorded were not adrenolytic effects but rather the central stimulant effects which are also known actions of these drugs. Maybe the findings can be taken to indicate that the adrenolytic and the stimulatory effects are only two sides of the same action. The fact that most adrenolytic compounds have distinct central stimulant effects of course supports this assumption.

The effect of norepinephrine is also of interest in this connection. When the blood pressure effect of epinephrine was high (generally in the emotionally unreactive cases), the blood pressure effect of norepinephrine was low. On the other hand, when heart rate increased less with epinephrine (or actually decreased), it also decreased more with norepinephrine—a reaction in the same direction. It has to be said that despite high correlation coefficients these correlations and intercorrelations are not always significant because of the small number of cases used in the epinephrine and piperoxan experiments. This cluster of results, particularly with drugs acting on the adrenergic system, however, seems to be the most promising outcome of our preliminary study.

The only autonomic drug which did not give any correlation with emotional reactivity in this study was methacholine. This is especially surprising as this drug is so widely used as a test drug in psychiatry.

This work is now being continued on a larger scale. Some changes have, however, already been made in the autonomic tests. The norepinephrine does has been lowered to the same level as the epinephrine dose (from 0·25 to 0·20 γ per kg/min), and this experiment now follows the epinephrine experiment in the same session. In another session the methacholine experiment is followed by the atropine experiment. The dose of atropine has been increased to 0·04 mg/kg. The piperoxan dose has been increased

from 0·25 to 0·35 mg/kg, and we feel that a further increase would not be impossible. The psychological stress experiments have also been modified.

On the whole, this pilot study seems to show that the effects of various autonomic drugs, especially those affecting the adrenergic system, are promising tools for research in the psychophysiological field. They can probably help to clarify states of increased or decreased autonomic activity levels, and also elucidate the connection between autonomic and emotional reactivity.

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VOL.
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EFFECTS OF HANDLING IN THE ADRENALECTOMIZED RAT TREATED WITH CORTICOSTERONE*†

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(*Received* 16 *December* 1960)

WE HAVE previously shown that, in the normal young albino rat, human handling enhances learning ability (BERNSTEIN, 1952; BERNSTEIN, 1957), and increases resistance to certain forms of stress (WEININGER, 1954; BERNSTEIN, 1956). More recently, we have shown that these effects of handling do not occur in the adrenalectomized rat (ELRICK *et al.*, 1958). These findings suggested that some hormone or hormones of the adrenal cortex or medulla are necessary for the enhancing action of handling on learning ability and resistance to stress. Corticosterone has been identified as the major adrenocortical steroid secreted in the rat (BUSH, 1953; HECHTER and PINCUS, 1954). The purpose of this study was to determine whether corticosterone would restore, in the adrenalectomized rat, the enhancing effect of handling on learning ability and resistance to stress.

METHODS AND MATERIAL

Three consecutive experiments were performed. A total of 84 male rats, Wistar strain (Charles R. River Breeding Laboratories, Wilmington, Mass.) were used: 24 animals in Experiment 1 and 30 animals each in Experiment 2 and 3. In all three experiments total adrenalectomy was performed on the 20th day of life. On the following day the animals were weighed and assigned at random to one of two groups for each experiment: a control (unhandled) group and an experimental (handled) group. Animals were placed individually in wire cages (measuring 20 × 17 × 24 cm) arranged in racks so that handled and unhandled animals were horizontally alternated. To avoid handling, the animals were weighed weekly in their cages and the weight of the cages subtracted. The temperature of the animal room was maintained at 80 ± 2° F.

A weighed amount of food in a special feeding cup (A. S. Aloe and Co., St. Louis, Mo.) which minimized spillage, was placed in each cage and left-over food was weighed daily to determine individual food consumption. The animals were fed powdered Purina Laboratory Chow (Ralston Purina Co., St. Louis, Mo.) and given 5% sugar in isotonic saline as drinking water. The corticosterone§ was given orally, mixed either with the food or the water. The corticosterone concentration used in Experiments I and II was at the lower level of adrenocortical steroid rate in the rat as reported by BUSH (1953), 8 mg/kg of body weight per 24 hr, and mixed with the Purina diet, 45 γ per g of food. In Experiment 3 the corticosterone concentration used was 24 mg/kg of body weight per 24 hr, the highest level of adrenocortical steroid secretion rate (BUSH, 1953). In this experiment, the corticosterone was added to the sugar-saline drinking solution.

In all experiments, beginning on the 21st day of life, each animal of the experimental group was handled individually for 10 min per day at the same time of day, for a period of 4 weeks. In each experiment a single, but different, investigator handled the animals. Handling consisted of holding the animal in one hand and stroking it repeatedly with the other hand from head to tail, with the animal facing the handler. Control animals were never touched after their original placement in cages.

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§ The corticosterone for all experiments was generously donated by Dr. Elmer Alpert, Merck, Sharp and Dohme Research Laboratories, West Point, Pa.

VOL.
5
1960/6

Following the 4 weeks of handling, the animals in all experiments were tested on a black-white discrimination problem. The apparatus was a T-shaped discrimination box shown in Fig. 1 and described elsewhere (BERNSTEIN, 1957). Either arm of the T could be lighted. Reward in the form of a bite-sized food pellet was always left in both food compartments. Each animal was introduced into the maze without handling, and was not handled at any time during or following the test. The training was light positive. At the choice point, the animal could make a correct choice or an error. An error was considered to have been made if the animal's body, exclusive of tail, entered the unlighted

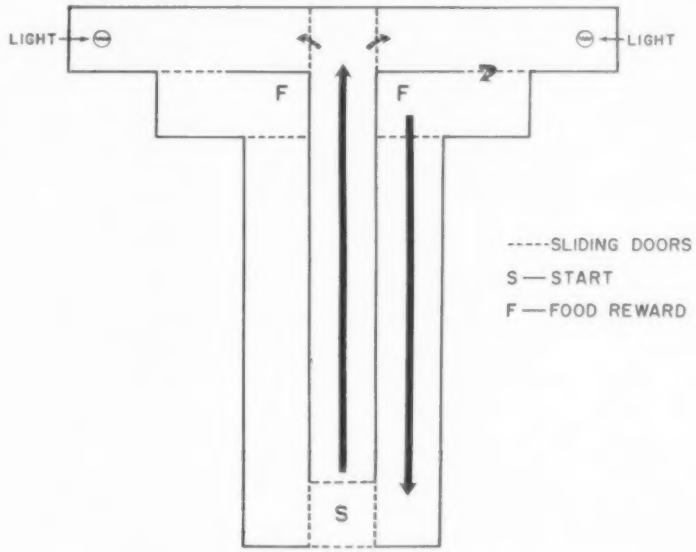

FIG. 1. T-shaped discrimination box. Floor plan of the apparatus.

arm of the T. The sequence of trials for the alley was LRRLLRLRRL* for the odd tens of trials and RLLRRLRLLR for the even tens. Each animal was given 5 trials a day for the first 2 days and 10 trials a day thereafter. The criterion of learning was reached when the rat completed 19 errorless trials out of 20 on 2 consecutive days. All animals were given at least 100 trials, in order to compare error scores.

When all animals had completed the discrimination learning test, they were tested on a shock-escape learning problem (BERNSTEIN *et al.*, 1960). The apparatus for this test consisted of a wooden box with a glass front and a grid floor (see Fig. 2). The box was 100 cm long, 18 cm wide and 46 cm high. The grid floor was 96 cm long. The grid was constructed of steel bars 0·32 cm in diameter spaced 2 cm apart. A continuous 60 cycle square-wave shock was supplied to the grid by an Applegate Model 228 stimulator set at 250 D.C. microamperes. An interval relay served to alternate the current so that every other bar of the grid was charged every second. A flat plexiglass plate, 10 × 12 cm was fitted over the center of the grid. Each animal was given five 1-min trials and was introduced at the opposite end of the apparatus on alternate trials. During each 1-min trial, the animal was free to move about on the grid, or to remain on the plexiglass plate, where it escaped the electric shock. The measure of learning was the time spent on the escape-plate during the 5 trials.

After the shock-escape learning test was completed animals of Experiments 1 and 2 were tested for resistance to a single intraperitoneal dose (50 mg/kg of body weight) of thiourea, as described elsewhere (BERNSTEIN and ELRICK, 1957). The mortality 24 hr after the administration of thiourea was recorded.

All statistical analyses were done by the use of the Mann-Whitney *U* Test, a non-parametric method (SIEGEL, 1956).

* L = left. R = right.

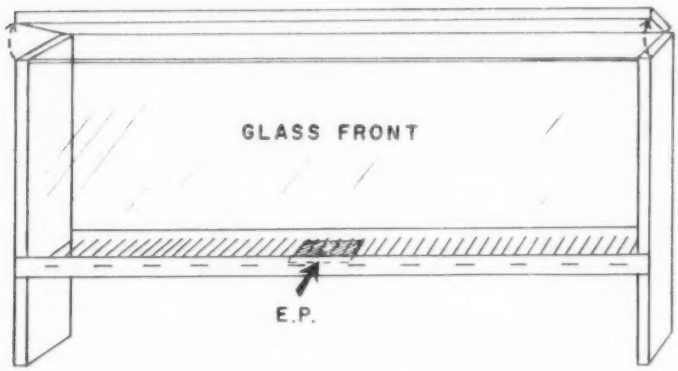

FIG. 2. Shock-escape apparatus. E.P. = escape plate.

RESULTS

Table 1 contains data from all three experiments. In each experiment on the discrimination learning problem the handled group reached the criterion of learning with fewer number of trials than their respective unhandled controls. Furthermore, in all experiments, the handled animals committed significantly fewer errors during the first 100 trials.

Although there was no significant difference between handled and unhandled animals on the shock-escape problem, there was a trend in favour of the handled groups. There was no significant difference in mortality rate between control and experimental animals following a toxic dose of thiourea.

In Experiment 2 the ratio of weight gain per g. of food consumed was significantly greater in the handled group as compared with the unhandled controls. However, in the other two experiments there was no significant difference between the two groups. These results parallel our findings in the normal rat (ELRICK, *et al.*, 1958).

A group of untreated adrenalectomized rats was used as an additional control in Experiments 2 and 3. The mortality in this group was 47 per cent as compared to 19 per cent for the corticosterone-treated animals.

Fifteen per cent of all the animals used in these experiments had small amounts of residual or regenerating adrenal tissue. These animals were eliminated from the analyses of the data.

DISCUSSION

Human handling leads to a significant improvement in learning ability in the normal young rat, as tested by a black-white discrimination problem and a shock-escape test; these effects are eliminated by adrenalectomy (ELRICK, *et al.*, 1958; BERNSTEIN and ELRICK, 1957). In the present experiments, handled young adrenalectomized rats, treated with physiologic quantities of corticosterone, were significantly superior on the discrimination learning problem to the corticosterone-treated adrenalectomized rats who were not handled. On the shock-escape learning test, there was a trend in favor of the handled groups, but it did not reach statistical significance.

The difference in the results between the discrimination learning and the shock-escape learning may be due to the difference in the nature of the two tests. In the

VOL.
5
1960/6

PSYCHOL.
19/61

TABLE 1.—EFFECTS OF HANDLING ON THE ADRENALECTOMIZED RAT TREATED WITH CORTICOSTERONE

Experiment No.	1 (Summer 1959)*			2 (Autumn 1959)*			3 (Winter 1960)*		
Group	Not handled	Handled	*P*	Not handled	Handled	*P*	Not handled	Handled	*P*
No. rats:									
Initial	12	12		15	15		15	15	
Final	11	10		11	13		11	13	
Mean food consumed (g) per animal	333·1	323·2	0·32	271·1	265·1	0·39	278·5	247·2	0·06
Mean weight gain (g)	162·3	156·1	0·21	126·6	136·7	0·25	120·3	106·5	0·11
Food consumed (g) per g weight gained	2·07	2·08	0·47	2·23	1·93	0·01	2·36	2·39	0·43
Maze learning:									
No. animals tested	11	10		11	13		11	13	
Mean trials to criterion	159·0	110·0	0·01	170·0	132·3	0·04	170·0	140·7	0·03
Mean errors first 100 trials	42·3	29·7	0·01	54·7	35·2	0·02	44·1	36·1	0·03
Shock-escape:									
Mean seconds on escape-plate	51·5	69·9	0·20	101·3	109·4	0·36	74·2	99·3	0·13
Thiourea toxicity:									
No. animals tested	11	10		11	13				
Mortality	10	8	0·46	10	11	0·48			

* Time experiment was done

shock-escape problem, there is continuous painful stress, with no food reward; whereas in the discrimination learning test, no painful stimuli are involved and there is a food reward for each trial. It appears that some other hormone or hormones are needed to restore the effect of handling on shock-escape learning. Similarly, injection of toxic doses of thiourea is more closely related to the shock-escape test than to the discrimination learning task.

The results indicate that corticosterone is required to elicit the enhancing effects of handling on certain forms of learning ability in the adrenalectomized rat. The specificity of corticosterone in this phenomenon remains to be determined. Further studies will be necessary to establish whether other adrenal hormones, such as cortisone, aldosterone, 17-hydroxycorticosterone, epinephrine, etc., have a similar or different effect.

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VOL.
5
1960/6

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THE PREDICTION OF PHYSIOLOGICAL RESPONSIVITY FROM PSYCHOLOGICAL RESPONSIVITY

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MANY physiological differences among psychiatric patients and between psychiatric patients and normals have been reported. Frequently these findings have been interpreted as support for an "organic" etiology of a particular psychiatric syndrome. Such interpretations have been particularly common in schizophrenia. The premises underlying the current study are that many such differences are expressions of differences in total responsivity and that psychological measures of responsivity will parallel physiological ones, independent of diagnostic group. From these premises we evolved and tested the hypothesis that a diagnostically heterogenous group of psychiatric patients who were rated as psychologically hypo-responsive would show less blood pressure response to mecholyl than would normal controls and patients rated as psychologically hyper-responsive.

Although the Funkenstein test has previously been utilized in innumerable studies and correlated with such variables as diagnosis [2], age [10], prognosis [1, 2] change in clinical status [3], perception [13], and capacity to abstract [8], it has not been used to test directly the present hypothesis. King's study of differences between the responses of "process" and "reactive" schizophrenic patients has possible relevance, however [6]. He found that process schizophrenics were less responsive than were reactive schizophrenics, since process schizophrenics generally are also less responsive psychologically, this finding is in keeping with our thinking. Similar findings have been reported by Geocaris and Kooiker [4].

Research which utilized other physiological measures of the response to stress has also yielded results in keeping with our hypotheses. Only a few illustrations can be cited here. It has been reported that the more chronic a schizophrenic illness the less adenosinetriphosphate activity in response to insulin [5]. Similar pathological blood sugar curves on the levulose tolerance test were obtained in schizophrenics, depressions and mania [9]. Anxious (hyper-responsive) subjects excrete greater amounts of hippuric acid as compared to controls and revert to normal levels with successful treatment [12]. Anxious subjects excrete larger quantities of hydroxycorticoids in response to corticotropin than do normals [11]. Anxious patients were hyper-responsive to pain stimulation on a number of physiological measures and the degree of physiological hyper-responsivity was correlated positively with the degree of anxiety [7]. The same study showed great resemblance between acute schizophrenics (hyper-responsive) and anxious subjects.

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METHOD

The present research was part of a larger project designed to investigate differential organismic reactions to a series of stimuli. An appropriate accommodation period preceded each stimulus yielding a cumulative accommodation curve over an hour and a half period. The findings to be reported are concerned with blood pressure responses to the injection of mecholyl. Psychiatric patients selected from both in and out patients facilities and who were not under somatic or pharmacologic therapy were interviewed by two experienced clinicians. Immediately following the interview each patient was rated on a seven point scale of "responsivity" ranging from relatively profound hypo-responsivity to marked hyper-responsivity. The ratings were made on the basis of intuitive clinical evaluation with no prediscussion between examiners. The clinical interviews were open-ended and relatively unstructured with regard to content. Each interview lasted about 15 min and all interviews were carried out by the same two examiners throughout the study. Inter-rater reliability was found to be 0·739 when the criterion for agreement was set at not more than one point difference between examiners. Only patients who met this criterion were included in this study; 7 patients failed to meet the criterion and were therefore excluded. Specific psychiatric diagnosis was not considered in the selection of patients. Physical contraindications to the administration of mecholyl excluded some potential subjects. A few patients had to be eliminated because their extreme hyper-reactivity and/or fearfulness resulted in their inability to cooperate with the measurement process.

In all cases the psychological ratings were made on the same day and prior to the physiological recording. In most instances patients were rated within one hour of the testing.

This procedure resulted in the identification of two experimental groups, 15 subjects rated as hypo-responsive and 23 subjects who had been rated as hyper-responsive. Thirteen volunteer hospital employees who had not been evaluated clinically served as a control group. Throughout the selection process matching for age and sex was attempted and statistical analysis established the three groups as homogenous with regard to these factors.

PROCEDURE

Following a uniform accommodation period serial blood pressures were recorded at 1-min intervals until five successive readings were obtained in which there was no more than 4 mm Hg variation. Following definition of this baseline 10 mg of mecholyl chloride were injected subcutaneously. Fifteen seconds after mecholyl administration a blood pressure recording was obtained followed by two more 15-sec readings. A series of ten 30-sec readings followed. Thereafter, blood pressure was recorded at 1-min intervals to complete a total post-mecholyl period of 25 min.

RESULTS

The blood pressure response was represented graphically and, with the use of a planimeter, a measurement of time-amplitude area of deviation from the baseline for the full 25 min post-mecholyl period was derived. Areas were measured in relation to a baseline derived from all accommodation periods. Since blood pressure deviations both above and below the baseline were considered as disturbances in

homeostasis due to mecholyl, measurements above and below the baseline were added together.

It should be emphasized that the conceptual framework in which the present hypothesis was formulated is concerned with responsivity rather than with general activity level. Stated in terms of current psycho-physiological terminology our hypothesis refers to response levels rather than to initial values. Thus the finding that there were no significant differences for the pre-mecholyl blood pressure values among the three groups highlights the response differences which were revealed.

A *t*-test of the physiological reactivity differences between the group rated high in psychological responsivity and the group rated low in psychological responsivity tends to confirm our hypothesis. The mean reactivity value for the hypo-responsive group was 2·43 in^2 with a standard deviation of 1·20. For the hyper-responsive group the mean value was 3·37 in^2, with an S.D. of 1·33. This difference is significant at the 0·01 level of confidence. The mean reactivity value for the control group was 2·91 in^2 with a S.D. of 1·55. This value is intermediate between the two experimental groups but not significantly different from either.

DISCUSSION

These results must necessarily be viewed with caution. The differences between the psychologically hypo-responsive and psychologically hyper-responsive groups depend upon the exact procedures described. Significant differences were not obtained when a different means of calculating the resting level of blood pressure was used (Hypo-responsive, 3·51; S.D., 2·64: Hyper-responsive, 3·68; S.D., 1·64; $t = 0{\cdot}195$) or when amplitude alone was compared with the psychological ratings (Hypo-responsive, 20·67; S.D., 9·17: Hyper-responsive, 19·59; S.D., 5·88; $t = 0{\cdot}443$). In addition only one physiological measure was employed and it is possible that similar differences would not obtain for other physiological measures. This possibility is being explored in work currently in progress. It is also true that, while the group rated as psychologically hyper-responsive was composed of most diagnostic groups, the group rated as hypo-responsive contained only chronic schizophrenics and retarded depressives. The differences obtained might therefore be a function of the latter two diagnostic groups only. This is a possibility which is difficult to check, because, as might be guessed, it is difficult to find other diagnostic groups for whom hypo-responsivity is characteristic.

On the other hand, our findings are lent greater weight by the fact that it was not feasible to test the most hyper-responsive patients because they could not cooperate in the procedure. If it had been possible to test this extreme group, it is likely that the magnitude of difference would have been even greater than that obtained here.

With the foregoing qualifications in mind, we interpret our findings as lending tentative support to the experimental hypothesis and to the conceptual premises underlying it. In this light the numerous physiological differences among various diagnostic groups are functions of the particular phase of adaptational effort rather than pathognomonic for diagnostic groups. This would possibly account for the extreme differences often reported within particular diagnostic groups, such as schizophrenics. This scheme would lead us to predict that any patient in any diagnostic group who is acutely anxious and struggling to adapt psychologically would reflect this struggle in a parallel physiological hyperactivity; conversely, any patient who had attained a psychological equilibrium by partial withdrawal from his environment

would not only be relatively unresponsive psychologically but physiologically as well. In addition to the broader implications of the study, we believe that this work underscores the need for careful description of the psychological parameters, beyond a simple diagnostic classification, of any patients who serve as subjects in research designed to elucidate psycho-physiological relationships.

SUMMARY

The present study is rooted in the premise that psychological measures of responsivity will parallel physiological ones in psychiatric patients regardless of diagnostic groups. The hypothesis tested was that a diagnostically heterogenous group of patients who were rated as psychologically hypo-responsive would show less blood pressure response to mecholyl than would patients rated as psychologically hyper-responsive.

Two experimental psychiatric groups rated as hypo- and hyper-responders and a control group of non-psychiatric volunteers were subjected to an identical series of physical stimuli including mecholyl injection. Although the pre-mecholyl blood pressure levels did not differentiate the groups, significant response differences were found in the predicted directions for the two experimental groups with the control group falling in an intermediate position. These findings are interpreted as additional evidence that psychological and physiological responses are inseparable parts of a unitary process of adaptation.

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VOL.
5
1960/6

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AN INVESTIGATION OF SOME RELATIONSHIPS BETWEEN VARIOUS MEASURES OF GALVANIC SKIN RESPONSE*†

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THE present study was undertaken to evaluate and compare some measures of conditioning and to relate G.S.R. conditionability to the level of background activity. We, as well as others (BURCH and GREINER, 1960; LACEY and LACEY, 1956; MARTIN, 1960), have observed that subjects differ in the amount of spontaneous G.S.R. activity shown under conditions of rest. Spontaneous activity is here defined as G.S.R. fluctuations that appear in a random manner and cannot be related to any specific stimulus. We had in earlier experiments observed that subjects who showed little or no spontaneous activity conditioned more poorly than those who showed such activity. MARTIN (1960) in a recent publication demonstrated that when spontaneous variations in palm to palm skin resistance are correlated with the number of conditioned responses, a high correlation, (0·62, significant beyond the 0·01 level) was obtained. Our investigation, although conducted independently and without knowledge of her procedure, may be considered as an extension of her study. We will, therefore, review the pertinent material from her study in some detail.

In Martin's study subjects were conditioned to a dim light (C.S.) in association with a loud tone (U.C.S.) with a C.S.–U.C.S. interval of 5 sec. Thirteen conditioning and 13 extinction trials were given, with an unspecified number of "adaptation" trials (to extinguish the unconditioned G.S.R. response to the C.S.). Spontaneous responses were defined as any deflection of 2000 ohms or greater occurring during conditioning but in the absence of any external stimulation. Her conditioned responses were apparently any response occurring during the presentation of the C.S. We suspect, therefore, that her conditional responses were orienting responses to light rather than true conditional responses (STEWART *et al.*, 1961). The orienting response is here defined as the unconditioned G.S.R. to the conditional stimulus. It is ". . . the response of the individual to a novel situation without special properties except that it is unusual in the recent experience of that individual and without previous specific connections, e.g., a noise, sudden light or unexpected touch. Such a stimulus produces a focusing of attention and movements, the orienting reflex of Pavlov or the questioning response of Whitehorn. An increase of respiration and of heart rate follows . . ." (LACEY and LACEY, 1956). Martin may well have been describing the G.S.R. component of the orienting response, which, as we have previously shown, returns when the C.S. (to which the orienting response has been "adapted" by successive presentations of the stimulus) is paired with a second stimulus (the U.C.S. being one of the class of stimuli) (STEWART *et al.*, 1961).

METHOD

Apparatus

The apparatus used consisted of a Fels-Dermohmeter connected to an Esterline-Angus chronograph (for recording G.S.R.), a series of three Hunter-silenced electronic timers (to program presentation of C.S. and U.C.S.), an Eico audiogenerator with suitable earphones, and a shock generator.

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The subject sat in a comfortable chair in a room adjoining the recording equipment. G.S.R. electrodes (supplied with Fels-Dermohmeter) were placed on the left palm and dorsum. Shock electrodes (standard E.K.G. electrodes) were placed on the subject's right ankle, and the headphones were placed over her ears. After a 5-min rest period the experimental procedures were initiated. All subjects were given a uniform introduction to the experiment and were not told that they would receive a shock. Since these subjects were acquainted with each other we asked them, at the end of the experiment, not to tell their fellow students what transpired in the experimental session.

Procedure

In our experiments the conditional stimulus was a tone of 500 c/s presented binaurally at an intensity of 65 dB above normal hearing threshold. The unconditioned stimulus was an electric shock of 2 mA presented through E.K.G. electrodes attached approximately 2 in. apart and 2 in. above the right ankle. The experimental sequence consisted of 20 adaptation trials during which tone only was presented at random (but predetermined) intervals. Twenty conditioning trials in which the C.S. was presented for 6·5 sec followed 1 sec after termination of the C.S. by the U.C.S. which lasted for 0·5 sec. Again, the interval between conditioning trials was randomly but consistently (between subjects) varied, the inter-trial intervals varying between 20 and 60 sec. Immediately following conditioning 20 extinction trials were given.

Subjects were a group of 19 student nurses. All were subjected to 20 adaptation trials. Thirteen were subjected to 20, and 6 to 40 conditioning trials (100 per cent reinforcement). All were subjected to 20 extinction trials.

The measures utilized were as follows:

(1) *Adaptation (to tone) period*

(a) *Spontaneous fluctuations.* All fluctuations between tone presentation trials of an amplitude greater than 500 ohms were tallied as spontaneous fluctuations. Since the time interval for the adaptation period was constant for all subjects no correction for time was necessary.

(b) *G.S.R. response to tone. (Orienting response)* The measure consisted of the number of tone presentations to which a G.S.R. was given between 1·5–4·5 sec (range) after initiation of the tone stimulus. The deflection, in order to be counted as a response had to be of an amplitude of 500 ohms or greater and had to be greater than spontaneous fluctuations occurring in the 5-sec period immediately preceding tone stimulation.

(2) *Conditioning period*

(a) *Spontaneous fluctuations*—same as during adaptation.

(b) *Response to tone*—same as during adaptation.

(c) *Anticipatory response.* This response, again had to be of an amplitude greater than 500 ohms and had to occur outside the range of the response to tone. Its (upper) limit was set at 1 sec after presentation of shock since the latency of the response to shock fell between 1·9–2·6 sec after initiation of the shock stimulus.

(3) *Extinction period*

(a) *Spontaneous fluctuations*—same as during adaptation.

(b) *Response to tone*—same as during adaptation.

(c) *Anticipatory response*—same as during conditioning.

(d) *Response to shock*—This response had to be of an amplitude greater than 500 ohms and had to occur within the range of latencies of the unconditioned response to shock.

(4) *Latency measures*

(a) *Response to tone during adaptation phase.* This measure consisted of the mean latency (per person) of the trials on which he gave a response.

(b) *Response to tone during conditioning.* Same as during adaptation.

VOL.
5
1960/6

(c) *Anticipatory response during conditioning*. Mean latency (per person) of the trials on which he gave an anticipatory response.

(d) *Response to shock*. Mean latency (per person) of the trials on which he responded to the shock stimulus.

RESULTS

The results for both the adaptation and the conditioning periods are based on the total subject sample ($N = 19$). Since 6 subjects had received 40 conditioning trials the results for the extinction period are based on the 13 subjects who had received an equal number (20) of conditioning trials.

Pearson product-moment correlations were computed for the set of latency measures as well as for the other three groups of measures. Rather than presenting the correlation matrix as a whole we have broken it down into meaningful groupings of intercorrelations which are described below. Tables 1, 2 and 3 depict these correlations.

(a) *Relationship of measures of spontaneous fluctuations to each other* (Table 1a)

TABLE 1.—CORRELATIONS (PRODUCT-MOMENT) BETWEEN SPONTANEOUS G.S.R. RESPONSES AND OTHER G.S.R. MEASURES

		Spontaneous fluctuations during		
		A	C	E
(a) Spontaneous fluctuations during	A	X	0·18	0·05
	C		X	0·56*
	E			X
(b) Response to tone during	A	0·68†	0·18	0·05
	C	0·50*	0·69†	0·44
	E	0·67*	0·67*	0·73†
(c) Anticipatory response during conditioning	A	X	X	X
	C	0·55*	0·84†	0·77†
	E	0·20	0·89†	0·54

* $P = 0·05$
† $P = 0·01$
A = adaptation period, C = conditioning period, E = extinction period.

Of the three correlations dealing with spontaneous fluctuations only the one between spontaneous fluctuations during conditioning and spontaneous fluctuations during extinction proved to be significantly correlated ($r = 0·56$). Thus if one can consider spontaneous G.S.R. fluctuations as a measure of "activation" or "drive state" (MALMO, 1959) it appears that the effect of the conditioning procedure produces differential levels of "activation" which cannot be predicted from "activation" at resting level. On the other hand when comparing the level of activation during conditioning and extinction one finds that an activating effect has taken place. Thus the increment in "activation" produced by pairing tone and shock is carried over into the extinction period. A future study will investigate whether this increment observed during extinction is a function of general sensitization or whether it is specifically related to the temporal patterning of tone and shock during the conditioning period, i.e., is a conditioned response.

(b) *Relationship of spontaneous fluctuations to response to tone measures* (Table 1b)

Of the nine correlations computed here six are statistically significant, three beyond the 0·01 level, three beyond the 0·05 level. The three highest correlations are, as were expected, those between the spontaneous fluctuations and response to tone during the same period. Spontaneous fluctuations during the adaptation period, correlated significantly with response to tone during all three phases of the experiment in which tones were presented; spontaneous fluctuations during conditioning were significantly correlated with response to tone during this and the extinction period, while spontaneous fluctuations during extinction were significantly correlated only with response to tone during the extinction period. Our data would thus suggest that spontaneous fluctuations under conditions of minimal activation correlate significantly with response to tone regardless of level of activation experimentally produced (through conditioning using shock as the U.C.S. in the present experiment). However, the converse is not true. Response to tone during adaptation is poorly correlated with spontaneous fluctuations under "activated" conditions.

(c) *Relationship of spontaneous fluctuations to measures of the conditioned anticipatory response* (Table 1c).

Spontaneous fluctuations during all three phases of the experiment correlated significantly with conditioned anticipatory responses during conditioning, the lowest correlation being with spontaneous fluctuations during the adaptation period. As far as conditioned anticipatory responses during extinction are concerned the only significant relationship obtained is with spontaneous fluctuations during conditioning, while that with spontaneous fluctuations during extinction just misses being significant at the 0·05 level. Thus we suspect that if one knew the level of "activation" produced by shocks of known intensity one would have a good predictor for conditionability.

(d) *Relationship between response to tone and conditioned anticipatory responses* (Table 2a).

Responsiveness to tone during both conditioning and extinction correlated significantly with conditioned anticipatory responses while response to tone during adaptation was only poorly correlated with it. Thus the cautious generalization put

TABLE 2.—CORRELATIONS BETWEEN RESPONSE TO TONE AND OTHER G.S.R. MEASURES

		Response to tone during		
		A	C	E
(a) Anticipatory conditioned responses during	A	X	X	X
	C	0·13	0·72*	0·76*
	E	0·08	0·54	0·55
(b) Response to tone during	A	X	0·22	0·37
	C		X	0·60†
	E			X

* $P = 0{\cdot}01$
† $P = 0{\cdot}05$
A = adaptation period, C = conditioning period, E = extinction period.

forth by REESE and DYKMAN (1960) that, "It is likely that the orienting response is an important indicator of 'conditionability' signifying that the organism is responsive and that a reflex pathway is available from afferents to efferents through intervening higher centers," (p. 253) is found to hold if the orienting response is evaluated during conditioning. However one cannot infer the organism's responsiveness during conditioning from a knowledge of the strength of the orienting response as measured under conditions of tone stimulation only. It would appear that a knowledge of spontaneous fluctuations is likely to be a better predictor of conditionability (as measured by the conditional anticipatory response) than response to tone.

(e) *Relationship of measures of response to tone with each other* (Table 2b).

The only significant relationship obtained was between response to tone during conditioning and extinction. This is essentially the same picture as that described for the intercorrelations of spontaneous fluctuations during the three phases of the experiment.

(f) *Relationship between "response to shock" during extinctions (a* C.R.*) and all other measures used.*

This conditioned response was not significantly correlated with either of the two measures used during the adaptation period ($r = 0{\cdot}31$ and $0{\cdot}25$ respectively for spontaneous fluctuations and response to tone). It also is not significantly related to the response to tone measure during conditioning ($r = 0{\cdot}45$), while it is significantly related to the five remaining measures (spontaneous fluctuations during conditioning ($0{\cdot}86$; $P = 0{\cdot}01$), spontaneous fluctuations during extinction ($0{\cdot}60$; $P = 0{\cdot}05$), anticipatory response during conditioning ($0{\cdot}80$; $P = 0{\cdot}05$) and extinction ($0{\cdot}78$; $P = 0{\cdot}01$) and response to tone during extinction ($0{\cdot}90$; $P = 0{\cdot}05$).

Looking at the data from another point of view one can ask the question as to what might be the best predictor for conditionability. We have used three measures of conditioning in the present study (anticipatory response during conditioning, anticipatory response during extinction and "response to shock" during extinction) and a fourth measure which simply combined the latter two. The highest correlations obtained are between spontaneous responses during conditioning and these various measures of conditioning ($r =$ of $0{\cdot}84$; $0{\cdot}89$; $0{\cdot}86$; and $0{\cdot}92$ respectively). Thus persons who show a relatively high level of "activation" *during* conditioning, condition best.

We suspect, along with SILVERMAN *et al.* (1959), BURCH and GREINER (1960), that within limits specific responses (G.S.R. responses to identifiable stimuli) and non-specific G.S.R. responses (spontaneous responses) parallel each other. According to these authors these limits are roughly placed between low level and "optimal" level of spontaneous G.S.R. fluctuations (or in Malmo's terms arousal or activation). Transcending "optimal" levels of spontaneous responsiveness produces a decrement in specific responses whether they are conditioned or unconditioned responses. From this framework it is apparent that the range of spontaneous responses of our subjects was within the low to "optimal" range.

It is not surprising that anticipatory responses during conditioning should correlate highly with the measures of conditioning used during extinction ($r = 0{\cdot}80$; $0{\cdot}80$; $0{\cdot}85$; with anticipatory response, response to shock, and sum of these two

measures) since one would expect that only if conditioning takes place would there be any response to extinguish.

(g) *Intercorrelation of latency measures* (Table 3)

Of the six possible intercorrelations three were significant beyond the 0·01 level. The three non-significant ones were between the conditioned anticipatory response and the other three measures. The three significant ones were those involving the correlations between the two responses to tone and the response to shock measure. Thus intercorrelations of latencies in response to stimulation are high while latencies to stimulation are poorly related to the latencies obtained for the conditioned response.

TABLE 3.—INTERCORRELATIONS OF LATENCY MEASURES

	Response to tone adaptation A	Response to tone conditioning B	Anticipatory response to conditioning C	Response to shock during conditioning D
A	X	0·67†	0·38	0·62†
B		X	0·37	0·76†
C			X	0·16
D				X

† $P = 0{\cdot}01$

DISCUSSION

The major finding of the present study concerns the relationship between spontaneous fluctuations of the G.S.R. and conditionability. A previous paper (STEWART *et al.*, 1961) discussed problems involved in defining the conditioned response in G.S.R. studies. We would like to reiterate that only the anticipatory response during conditioning and the anticipatory response and "response to shock" during extinction should be considered as conditioned responses. The response to the conditioned stimulus the "orienting" response (this response invariably returns after it has been "adapted out" when it is paired with the U.C.S.) should never be considered as such. This "orienting" response is the response that is usually of the greatest amplitude and is in most studies of G.S.R. conditioning referred to as the conditioned response. It is not a conditioned response because it (a) generally appears full-blown on the second or third conditioning trial (after a series of adaptation trials), and (b) shows the same curve of extinction (during conditioning) as seen in adapting out the response to the C.S. (See Fig. 1).

Our measure of spontaneous fluctuations in the G.S.R. is somewhat different from LACEY and LACEY's (1956) "frequency of skin resistance activity" measure. The latter used as their measure the number of half-minutes in a 15-min period during which bursts of skin resistance change greater than 600 ohms occurred. Our measure, on the other hand was a tally of the total number of deflections greater than 500 ohms that occurred during the period we were measuring spontaneous activity.

LACEY and LACEY discuss, at length, various possible interpretations of the spontaneous fluctuation phenomenon. The first is the idea that we are dealing with a chained succession of responses triggered by a known stimulus. The second is the notion that these fluctuations are stimulus produced chained responses, with the stimuli being either covert or undetected by the experimenter. Both these possibilities

VOL.
5
1960/6

are rejected by these authors in favor of simple "spontaneous activity". In these author's words, "The source of the autonomic oscillation is to be sought, not in adventitious stimuli, nor in fleeting disturbing ideation, but in physicochemical processes at the level of localized cell aggregates." (p. 163)

The fact that only in one of the two studies reported did the above authors demonstrate the reliability of this measure over time, (under resting conditions) might argue against this interpretation. Although this is a most elegant notion we

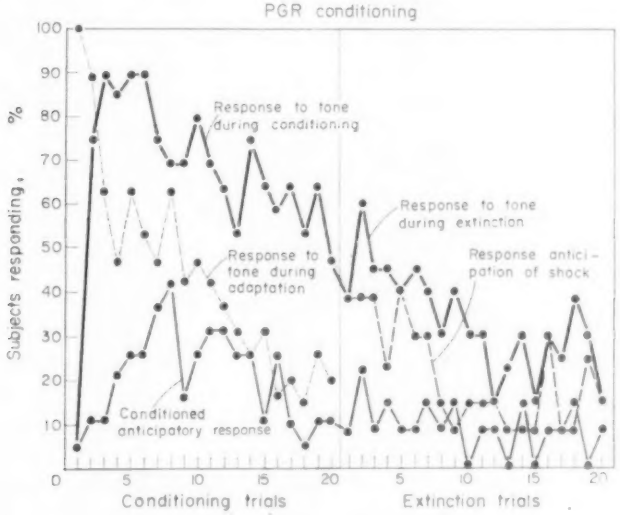

Fig. 1.

are at the moment loath to give up the idea that these responses are stimulus induced.

We would expect, on the basis of the idea that these responses are stimulus induced, that when recording G.S.R.'s in subjects going from wakefulness to sleep that there would be a similar decrease in the spontaneous fluctuations. Similarly, in going from a state of simple wakefulness to one of a high expectancy of fearful, painful, or unpleasant stimulation we would expect an increase in spontaneous responsiveness. Our observations as well as BURCH's (1960) results concerning the effect of pentothal, epinephrine and "anxiety" on non-specific G.S.R. responses seem to bear out this hypothesis. Pentothal, a sedative, lowered spontaneous fluctuations while both epinephrine and "anxiety" increased spontaneous fluctuations.

Again, LACEY and LACEY in looking at personality differences between the extremes in performance on their autonomic measures are willing to append the following labels to those with high and low levels of activity respectively—"manifestly anxious, hysterical, and overly reactive" for the former, "phlegmatic, repressed, resilient, lacking affect" (p. 164) in the latter. They quote BURCH *et al.* (1942) who related spontaneous fluctuations in peripheral blood flow to personality differences as stating, that those with small and limited spontaneous variations are placid and emotionally stable people who are little affected by disturbing environmental conditions while those whose peripheral blood flow is characterized by large fluctuations of

greatly variable magnitude are described as inquisitive and at times anxious about the experimental procedure and who reacted to their environment with fluctuations in mood. It seems to us that both these observations would again lead one to infer a stimulus produced effect to account for the observed spontaneous fluctuations. People who are inquisitive, anxious, and overly reactive would be expected to be more acutely aware of and responsive to events in their environment than is true of those characterized as phlegmatic, repressed, lacking affect, placid and emotionally stable.

Leaving speculations concerning the origin of "spontaneous fluctuations" we do find that both studies that have concerned themselves with this problem demonstrate relationships between such fluctuations and measures of "conditioning" (MARTIN and present study) as well as with measures of impulsive motor responses, voluntary control of response latencies, and reaction times (LACEY and LACEY, 1956).

Our study demonstrates that spontaneous fluctuations may well be an index of "activation" or "generalized drive state" since those subjects who showed a relatively high level of activation during the conditioning period were those who conditioned best ($r = 0{\cdot}84$) and also showed the least adaptation to tone stimulation ($r = 0{\cdot}69$). However, "activation" during conditioning, as well as the other measures obtained during conditioning, is only poorly related to "activation" measured during the adaptation period ($r = 0{\cdot}18$; $0{\cdot}22$; $0{\cdot}13$). Thus, under most experimental conditions prediction of conditionability or responsiveness based on resting measures of "activation" are most likely to fail. We suspect that the shock stimuli presented during conditioning, or the expectation of shock during conditioning had a differential effect on our subjects. Those who were most activated by such stimulation or the threat of such stimulation conditioned best.

We had thought that latency of the response to shock might prove to be a useful measure to evaluate the "strength" of the perceived electrical stimulus. To test this hypothesis we correlated this latency measure with number of anticipatory responses during conditioning and obtained a non-significant correlation of 0·19. Amplitude of the G.S.R. also does not appear to be related to "felt" intensity of the stimulus since subjects who show adaptation of the G.S.R. will persist in giving behavioral responses to shock stimulation.

SUMMARY

Various measures of G.S.R. were related to each other and to measures of conditioned G.S.R.s and the results evaluated within the "activation theory" framework.

The results indicate that:

(1) The orienting response to the conditioned stimulus reappears when the C.S. is coupled with the U.C.S. This response has in many studies been called the "conditioned response." It is not a conditioned response because it shows a curve of adaptation similar to that shown to the C.S. alone.

(2) Three measures of conditioning were defined, the anticipatory response during conditioning, the anticipatory response during extinction and the response to shock (in the absence of shock) during extinction. As expected these three measures correlate highly with each other (0·80; 0·80; and 0·78).

(3) Measures of spontaneous G.S.R. fluctuations under condition of "activation" by shock correlate highly with all measures of conditioning while spontaneous G.S.R fluctuations under conditions of relative rest (during tone stimulation period) correlate poorly with measures of conditioning.

VOL.
5
1960/6

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OL.
5
0/61

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AN APPARATUS FOR PUPILLOGRAPHY WITH INTERMITTENT INFRARED LIGHT*

INGMAR DUREMAN, TORKEL SCHOLANDER and HENRY SÄLDE

(*Received* 30 *November* 1960)

INTRODUCTION

DURING recent years the continuous registration of pupillary reactions to different external and internal stimuli has been accomplished chiefly by using two different principles, the photoelectric and the cinematographic.

The former method was introduced by Malthesos in connection with animal experiments and has been improved and developed by MATTHES (1941) and CÜPPERS (1951, 1954) for use in investigations with human beings. A similar method has been used by Russian scientists ATAEV (1953) and GLEZER (1953).

The foremost exponent for the cinematographic method has been LÖWENSTEIN (1942), who during more than thirty years of research has built up a large, complicated and very expensive apparatus.† MACHEMER (1941), and more recently PETERSEN, (1956) have simplified the method and tried to make it more adaptable to clinical use. His monograph is recommended for a more detailed historical survey.

Common to the methods mentioned here is the use of infrared illumination of the eye, which does not affect the pupil. Registration can thus occur even in the dark. The *photoelectric* method is built on the changes in the amount of reflected infrared light which is brought about by changes in pupillary size. These changes are then registered directly on paper or a film by means of a photocell. Thus, one obtains here an immediate and continuous registration of the course of the reactions. On the other hand, no information is obtained on the absolute size of the pupil. Neither is it possible to follow irregularities in the form and concentricity of the pupil during its course of movement. Thus, even though the method has many advantages because of the direct and continuous reading of pupillary reactions, this does not, in its present form, outweigh the disadvantage that quantitatively it is not correct.

By means of *cinematographic* registration a relatively accurate absolute measurement of the pupil is obtained, and it is also possible to follow any subsequent deviations in form and movement. The method is certainly not continuous, but since the film can be speeded up to 100 pictures per sec, in reality this makes little difference.

From the beginning we have endeavoured to work out a relatively simple and easy method which would involve the least possible discomfort for both the subject and the experimenter. Finally, there should also be possibilities for synchronization with other recordings of autonomic functions.

The last named pre-requisite soon forced us to give up the current cinematographic methods because of insurmountable difficulties. Instead we have constructed an apparatus with intermittent infrared illumination produced by a stroboscope. The film runs continuously without a shutter, with the help of two synchronmotors.

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† During the final preparation of this manuscript for publication we learned that a new device for electronic pupillography has been constructed. The underlying principle of this instrument is that it measures the time consumed by oscillographic scanning of the diameter of the pupil. A great advantage is that it gives a direct continuous tracing. LÖWENSTEIN O. and LOEWENFELD I. E. Electronic pupillography. *A.M.A. Arch. Opth.* **59**, 352 (1958).

VOL.
5
1960/6

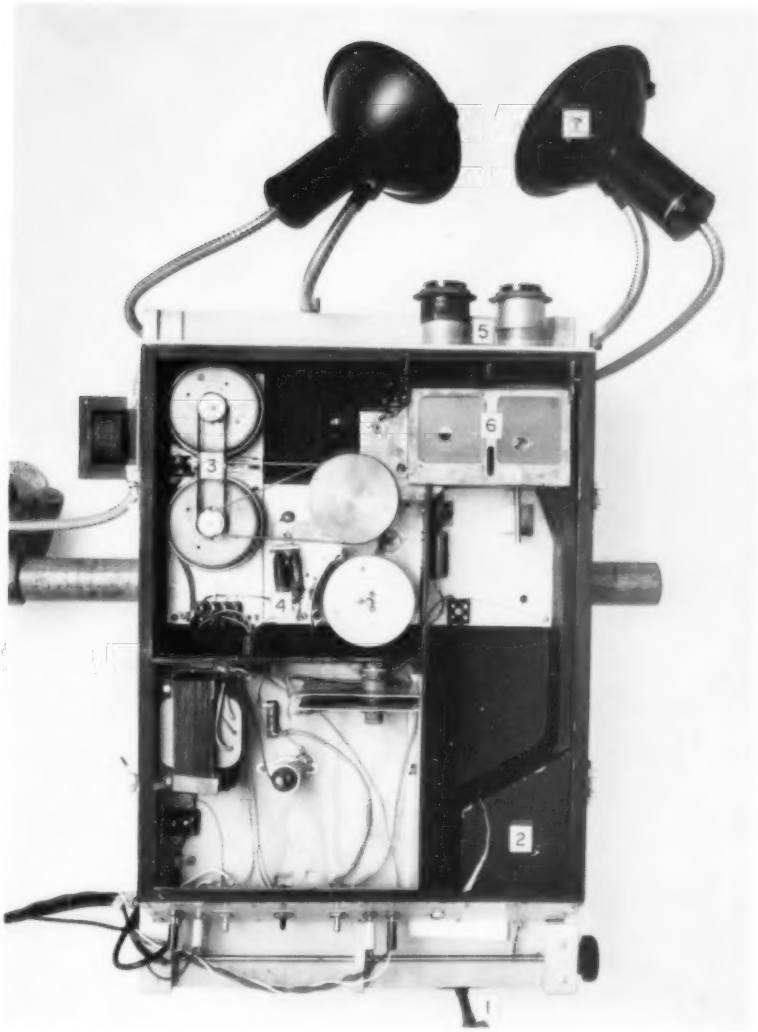

FIG. 1. View of the open camera. For further explanation of the figures, see p. 225.

VOL.
5
1960/6

There are many advantages with such a device; one is that both the stroboscope and the camera can be steered by the same timer which can even start possible simultaneous recordings. another is that there is no difficulty with the marking of time.

APPARATUS

The apparatus consists of two parts: (i) cine-camera [with a propelling device for the film], (ii) stroboscope and timer [with infrared flashtubes]. The camera is shown open in Fig. 1. It is mounted on an arm extending from a stable stand, which permits raising and lowering as well as swinging and displacement sideways. The camera is attached to a table with casters and can be moved toward and away from the subject (S) who sits in a comfortable chair with his head on a specially constructed head-rest which supports the head as firmly as possible without being uncomfortable. A little red twinkling bulb (1) on an adjustable holder attached to the camera, at a distance of 72 cm from S, serves as a fixation point. A simple sighting device permits S to control the focus during the experiment.

The camera box is made of plywood which has been lined with aluminium foil, and is painted black inside. The 35 mm film runs from a light-proof casette (2), and is driven continuously by a rubber spool with two synchronmotors (3). By means of an electromagnet (4) one can, either manually or via a timer, hold firmly or release the propellent rubber spool. The speed of the film is adjusted according to the preferred speed of exposure.

The two objectives (5), 80 mm Zeiss Tessar 1–2. 8, are mounted side by side on moveable plates, thus permitting an adjustment which corresponds to the distance between the pupils. The film runs horizontally, and when both eyes are photographed the objectives are placed so that the eyes are reproduced each on its half of the film. When photographing one eye, only one-half of the film is used and after it has been turned in the dark the other half can be exposed.

Precision focusing has been solved with a mirrorvisor device (6) so that the picture is thrown by way of a mirror upon a ground-glass at the time of focusing. Small, round, mutually displaced prisms are inserted in the ground glasses. These serve two purposes, viz. that of exact focusing, and that of correct placement of each eye on its half of the film. In focusing, the camera is moved until both eyes are in the right position and are reproduced sharply without breaks of the contours in the prism-sight. This distance is corrected for infrared wave length (PETERSEN pp. 102–103). While photographing the mirrors are pressed up by means of a catch.

Exposure takes place with two flash-tubes (7) which are coupled in series and are driven by a stroboscope with a very high output. When the frequency of exposure is pushed up towards 100 pictures per second, practical problems arise in connection with overheating. Thus it is necessary to arrange for air or liquid cooling of the flash-tubes. Moreover with such high speeds the voltage in the stroboscope must be much increased. If the condensers are not allowed to charge sufficiently between each flash, the result will obviously be a reduction in the light-intensity. With frequencies around 25–30 pictures per second, however, the generation of heat becomes negligible, during shorter periods of recording. The flash-tubes are mounted in adjustable projectors and equipped with a Kodak infrared filter no. 87. This effectively filters out waves shorter than 740 mμ, and the remaining infrared light does not affect the pupils. The film used is Kodak infrared super sensitive.

Up to this time reading of the films has been accomplished by means of a projector, which enlarges each picture to ten times its original size.

SUMMARY

An apparatus for pupillography which is simple and easy to handle and therefore adaptable to practical clinical purposes is described. The registration is cinematographic, but the film runs continuously without a shutter with the help of two synchronmotors. The infrared illumination is intermittent and produced by a stroboscope.

Acknowledgements—Fredrik Backlund, M.A. and our technician Martin Juhlin have managed the construction of the apparatus. Without their invaluable assistance and never failing interest this work would have been impossible.

Our work has been supported by grants from the Swedish Medical Research Council. A special

grant given to one of us (Dureman) by the Västerås Board of Culture made it possible to make invaluable direct contacts with German experts on pupillography.

The subsequent refinement of the method through experiences obtained during large-scale practical application would have been impossible without generous support from the Swedish Malt Beverages Research Council and Syster Thânell's Fund for Psychiatric Research.

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VOL.
5
1960/6

Journal of Psychosomatic Research, 1961, Vol. 5, pp. 227 to 228. Pergamon Press Ltd. Printed in Northern Ireland

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VOL.
5
1960/6

J. Psychosomatic Res., 1961, Vol. 5, pp. 229 to 234. Pergamon Press Ltd. Printed in Northern Ireland

BOOK REVIEWS

FLANDERS DUNBAR: **Psychiatry in the Medical Specialities,** McGraw-Hill, London. viii + 535 pp. 93s.

THE late FLANDERS DUNBAR was a woman of indefatigable industry: the last edition of her classical Emotions and Bodily Changes runs to 1192 pages, and lists 5047 references. Her latest and possibly last book is a distillation of her encyclopaedic knowledge of the field, written in order to acquaint physicians and surgeons with the psychiatric aspects of disease. The psychosomatic approach to medicine is centuries old, although it has become eclipsed by the rise of scientific medicine and the startling advances resulting from this. Now there is a swing of the pendulum, and much is made of the virtues of a holistic approach. But what is to be the theoretical groundwork—psycho-analysis analytic psychology (hardly ever taken into account), existentialism, or psychobiology? This is the dilemma which the book poses so clearly. Are we to accept what the analysts have told us about asthma, ulcer, and other disorders, or such statements as "the cancer prone tend to be consistently serious, over-co-operative, over-nice, over anxious, painfully sensitive, passive, apologetic personalities and as far as could be ascertained from family, friends and previous records, they had suffered from this pitiful lack of self-expression and self-realisation all their lives." Of course it is easy to pick out an isolated sentence here and there for criticism, and this is far from being the purpose in this reveiw but the fundamental question the reader must ask is this—do we accept the tenets, postulates and formulations of a particular school? If we do, then the book will be an acceptable account of psychosomatic relations: if not, we will probably have some criticism for every page. Can a well-balanced book on the psychiatric aspects of disease be written for use by non-psychiatrists and, at the same time, be acceptable to psychiatrists? Here lies the difficulty which, unfortunately, this book does not solve. It is too personal a document (as such it is of great interest), it is too long, and certainly some of the ideas are too outrageous to be acceptable to the majority of non-psychiatrists. A satisfactory book has yet to be written on the topic Flanders Dunbar set herself.

DENIS LEIGH

The Meaning of Death. Edited by HERMAN FEIFEL, Blakiston Division, McGraw-Hill Book Co., Inc., New York, pp. xviii + 351, 50/6.

THE importance of grief, of death, and of separation is still all too little recognised by psychiatrists in their day to day work. Like their patients, it is hard to face up to the inevitability and ubiquity of death; medicine is devoted to life, to cheating death. The doctor imagines himself all too familiar with many forms of death, and indeed he is, in a matter-of-fact and casual way. But it is only when reading a book like this that the realisation comes of how little do we in fact square up to the inevitable end. Jung points out how the great religions, and particularly Christianity and Buddhism are "complicated systems of preparation for death"—death is the fulfilment of life's meaning, instead of just a mere cessation of being. Today it may be more often the doctor than the priest who has to deal with the anxieties and apprehensions of the individual in his approach towards the problems of death. Every psychiatrist will find something of interest in this collection of papers on death—there are contributions from Jung, from existentialism and from psycho-analysts, as well as cultural studies. Nor is religion, nor biology omitted from what is a most fascinating and erudite study of a subject which concerns us all so vitally in our practice, and in our own personal lives.

DENIS LEIGH

THEODORE C. KAHN and MARTIN B. GIFFEN: **Psychological Techniques in Diagnosis and Evaluation,** Pergamon Press, London, 1960. pp. xi + 164, 40s.

THIS book is a welcome relief from the formidable tomes the psychiatrist has come to expect from his psychological colleagues. It also fills a real gap—providing a simple, factual account of the different types of tests which can be usefully employed in the clinical practice of psychiatry. It will prove a boon to those taking up psychiatry, and to the physician with an interest in the psychological aspects of medicine. Considering the literally thousands of tests which exist, it would be easy to criticise the authors for the omission of this or that test—for instance, British readers will find no mention of Raven's Matrices, nor of the various tests developed at the Maudsley Hospital. But the whole approach is so sensible and modest, and the tests so well described that the book cannot be anything else but a success.

DENIS LEIGH

Ministerium Medici. (Edited by G. A. LINDEBOOM and R. EEG-OLOFSSON) Royal Vangorcum Ltd., Assen, The Netherlands.

THE aim and intention of this new periodical are unexceptionable to the Christian: "To create an organ of fellowship between Christian doctors and their national associations, also to find a place for common reflection on the ethical problems of our profession and the spiritual basis and background of our professional life."

Both its country of origin and the very high quality of its technical production are further favourable factors, combining a solid respectability with an impeccable presentation. But unless these initial assets are matched by a comparable vigour, originality, and imagination in the individual contributions, it will fail in its purpose and become just one more sponsored medico literary journal, vying with the glossy advertising products of the drug houses for space in the wastepaper basket.

The central philosophical problem inherent in a religious approach to medical experience is the contradiction between the creative love of God, and the innately destructive aspects of life: between the concept of grace and the life cycle of the malaria parasite. Sherrington's answer to this was essentially humanistic. The spiritual interpretation cannot afford to be less profound in its analysis, or less eloquent in its exposition.

Of the current items in this opening number, none essays the central problem: while the most ambitious and potentially profound, on the subject of death, is betrayed into tragicomedy by an execrable translation. Welcome, and warning, seem the reviewer's duty in this instance: guarded goodwill his prescription for future readers awaiting further editions.

D. STAFFORD-CLARK

JOHAN BREMER: **Asexualization. A Follow-up Study of 244 Cases,** Macmillan, New York and London, 1959, pp. 336, 35s.

THIS is a study, with followups, of 216 males castrated in Norway between 1935 and 1949, under the Norwegian Act of 1934 and the Nazi "protection of the race" enactment of the occupation. The age range at operation was 13 to 68 years; the psychiatric diagnoses were: oligophrenia (109), schizophrenia (53), sexual deviants and psychopaths (40), epilepsy (10). Of all these, 102 had been brought before the Courts as sex offenders. Not more than 3 per cent of sex offenders are castrated in Norway.

The object of the study was to determine the physical and mental (objective and subjective) consequences of castration, as well as the several indications for the operation and whether, from the therapeutic, judicial and administrative points of view, these were justified by the results.

VOL.
5
1960/6

Thoroughly carried out and cautiously assessed, the study is clarified by many tables and case histories which will enable the individual researcher to utilize the material for his own purposes. Although there are certain short-comings inevitable in a study which is largely retrospective, e.g. lack of continuous observation, reliances on the patient's anamnesis and on records which were collected without uniformity and not for research purposes, yet the study stands as a very valuable addition to the literature.

As to conclusions, "If castration is to have any effect it must be proved that the person has sexual urges, either strong or weak, but at least with an urge for sexual relief. It seems to be irrelevant what direction or manifestation the sexual urge has . . . ." The best results were obtained with habitual sexual deviants and with sexually disturbed oligophrenics. No general pacifying or sedative effects were noted in the psychoses, psychopathies or neuroses. No 'resocializing' effect occurs outside the purely sexual sphere, and castration has no therapeutic effect on constitutional, epileptic or schizophrenic psychoses.

The varying effects of castration on potency, libido and upon mental and physical states, will have particular interest for readers of this journal.

The last part of the book describes a similar study upon 28 legally castrated women. The results of castration were so uncertain and poor that the author doubts whether it has any justification.

P. D. Scott

OL.
5
0/61

Behaviour Therapy and the Neuroses. Edited by J. H. Eysenck. Pergamon Press, Oxford. 1960. p. XI + 479, 63s.

Readers of this Journal are already familiar with what is, to many, a new incursion into the treatment of the neuroses and psychosomatic illnesses, for some of the earlier work has already been published in this Journal. Now Professor Eysenck has gathered together and reprinted in one volume many of the previous reports, whilst members of his department have written some original sections, dealing for instance, with the treatment of writer's cramp, of tics, and nocturnal enuresis. Although Professor Eysenck, by his blunt, unequivocal and often somewhat aggresive turns of phrase arouses strong feelings in his psychiatrist colleagues, he is never dull, and in fact is a continual source of intellectual enjoyment, and stimulus. Much as some may disagree with the fundamental premises of behaviour therapy, there is no denying that here is a contribution from the psychologists that some of us have long awaited. Contact with these brilliant, clear minded young men, always ready to question, and to put to the test of experiment, is a privilege those of us working at the Maudsley Hospital greatly enjoy and benefit from. Viewed in the fierce light of clinical practice and experience, the application of Behaviour theory to treatment is far from convincing; nonetheless psychiatric treatment must always be subject to ruthless examination and criticism, and this is what Professor Eysenck and his colleagues are doing. However controversial their work, none of us can afford to dismiss it, and this book will be eagerly read and pondered on by all readers of this Journal.

Denis Leigh

Progress in the Biological Sciences in Relation to Dermatology. Edited by Arthur Rook, M.D., M.R.C.P. pp. xv + 480. Cambridge University Press, 1960, 84s.

The lectures and abridged versions of the discussions following them printed in this volume were given in the Post-Graduate Medical School of the University of Cambridge in the last week of September 1958. In a brief foreword Professor J. S. Mitchell stressed that 'the integration of medical science with clinical practice' has been since the days of Harvey 'one of the characteristic features of British medicine' and that the need today more than ever was to 'utilize to the full, the advances in the

scientific basis of medicine' which it was the aim of this course of lectures to furnish in dermatology. The programme covered a wide variety of subjects such as "Cutaneous Innervation," "The Histochemical Investigation of the Skin," "Immunology," "Inflammation," "Radiation and the Skin," "Pharmacology," but of greatest interest to readers of this Journal will be the four lectures and discussion on "Psychophysiological Mechanisms."

D. Russell Davis spoke on "Psychological mechanisms in psychosomatic disorders" with special reference to "the stereotyping of the reaction" so that "the pattern remains the same although the stressors which evoke the reaction vary," and raised the question "whether reactions served by the autonomic nervous system are learned in accordance with the principle of reinforcement, or whether it is necessary to suppose that their learning is governed by the law of association." This he saw as the crucial issue facing contemporary research into psychological mechanisms concerned in psychosomatic reactions since "If it can be answered, it will be possible to go on to answer the further questions: how do reactions persist and recur. . . ? And how can they be extinguished"?

In "Psychological mechanisms in the psychosomatic skin affections" J. H. Cullen stressed the "general concept of disease as a maladaptation between the organism and its environment" because of the "unfortunate implications of a body-mind dichotomy" inherent in the term "psychosomatic."

F. A. Whitlock reviewed critically "the psychosomatic concept applied to Dermatology" concluding that "Any attempt to make a given dermatosis the exclusive domain of the psychiatrist or the dermatologist is unlikely to succeed. The causes of these illnesses are manifold and so, I believe, are the cures." Brian Ackner described investigation of "The relationship between anxiety, alerting, and cutaneous vasomotor activity" by a combination of E.E.G. and plethysmographic recordings taken from emotionally disturbed and normal control subjects.

The discussion was enlivened by some refreshing free speaking by physicians about their experiences of psychosomatic disorders in "lunatics." Brian Russell "as a simple dermatologist" confided that he divided patients into "those who wish to get well and those who (unconsciously) resist cure" reminding one that in psychiatry perhaps as in no other specialty is it possible to throw the blame of therapeutic failure so squarely on the patient.

Although there is nothing very new in these pages their mixture of expressions of philosophical faiths and neurophysiological concepts, of behaviourism and Freudian terminology, of clinical observation and comparative psychology, illustrates the confusion, semantic and otherwise, which besets the subject, which no doubt arises not only from the lack of accepted psychiatric theory but also from trying to regard man or his psyche as his own pathogen. One gets the impression that advances in dermatology may greatly curtail the wide application of the psychosomatic concept in this field.

Ida Macalpine

Jerome M. Schneck: **A History of Psychiatry**, Charles C. Thomas, Springfield, Ill. 1960. pp. ix + 196, 44s.

The history of psychiatry has been comparatively neglected until recent years. The scarcity of original sources, and the pre-occupation with the administrative and legal aspects of psychiatry, as well as with the horrors of lunacy have all contributed to this neglect. Now psychiatry is flowing once more into the mainstream of medicine, and there is a resurgence of interest in the origins of our ideas. Ackerknecht's recent small and very compressed book was too telegraphic to be completely satisfying as an introduction to the subject, Altschule's book was more in the nature of a fascinating series of essays. Now Dr. Schneck has given us a book which seems wholly admirable as a general, compact outline of the subject. It will be useful for both medical student and psychiatrist alike. His bibliography is both selective and comprehensive, and his approach refreshingly free from any particular bias. The book is beautifully produced, and although the price may be high for European book-buyers, no doubt it is reasonable for the American market. It can be wholeheartedly recommended.

Denis Leigh

WM. MCCORD and JOAN MCCORD with JOHN GUDEMAN: **Origins of Alcoholism,** Tavistock Publications Ltd. 1960. pp. xi + 193. 35s.

THIS is a notable contribution to the scientific study of alcoholism, unique in its way. The authors are sociologists at Stanford University, who have exploited the raw material available from the Cambridge-Somerville Youth Study in admirable fashion. This Study provided data about more than 500 boys, growing up in Massachusetts in the late thirties, and included a control group. There has been a follow-up study which has revealed, among other matters, that some of these boys have become alcoholics, some criminals, with overlap between these two groups.

The present work analyses the differences in background of the non-criminal alcoholics, the criminal alcoholics, and the non-alcoholic criminals in terms of environmental and emotional factors.

These terms are clearly defined in the text, and the methods are given in detail in the appendix, with explanations and descriptions of the methodology. Whilst the measures are stated and correlated, justification for going beyond these to a more general theory of causation is adequately defended.

Interestingly enough, in the course of their analysis of the data, the authors find nothing to support the traditional Freudian view of the importance of oral fixations and homosexual leanings in the genesis of alcoholism.

The operational definition of alcoholism used here embraces men with two convictions for drunkenness. This is a long way off alcohol addiction, so that these two terms must not be confused in any wider conclusions drawn from this research.

Nevertheless this is a model of its kind, unlikely to be repeated for many years with other groups. Where they touch on current views of aetiology, the authors summarise these admirably and give references to important articles and reviews, so that those interested in this subject will find this book an excellent guide to many aspects of work on this widespread problem.

D. L. DAVIES

JOHN LANGDON-DAVIES: **Man: The Known and Unknown,** Secker and Warburg, London, 1960. pp. 226, 21s.

THIS book follows a pattern common to many works intended to persuade readers to belief in the incredible. At least half the volume consists of an exposition of popular science showing how, in the light of ever accummulating factual observations, old fashioned scientific models, and especially mechanical models, prove to be inadequate and have to be replaced by different concepts. "What has made it impossible for the physicist any longer to have a mechanical model of the atom is that you cannot have a model without substance, and substance has, as a result of experimental research, been dismissed from the atom, leaving nothing behind except varying concentrations of energy." (p. 54).

That it is dangerous to dogmatize about wide philosophical issues, such as mind-matter relationships, on the basis of the current fashion in experimental hypotheses, is a moral with which few would nowadays disagree. Unfortunately the open-mindedness thus stimulated is at once exploited to persuade the reader into accepting as scientifically plausible such concepts as telepathy, mediumship, faith healing and even perhaps survival of the individual after death. The line of reasoning seems to be that we have hitherto regarded these matters as incredible solely because they violated the implications of some scientific models that have recently become out-moded.

In point of fact, people are probably less influenced by theoretical difficulties than by the elusiveness of the alleged phenomena, and the unconvincing nature of much of the evidence. On the level of experimental evidence Mr. Langdon-Davies offers nothing new, and a somewhat indifferent selection of what is already on record. The well known difficulty that when psychic experiments are repeated they almost invariably produce no result is dismissed with the airy comment that you cannot duplicate the necessary conditions. An account of the author's personal experiences in card guessing under poorly controlled conditions, a few quotations from reports on the nineteenth century medium Mrs. Piper, and some speculations on paranormal healing devoid of any actual case, comprise the bulk of the section on the supernormal. This is unlikely to convert any sceptics, and it will certainly irritate specialists in the field, who have put much effort into sorting the wheat from the chaff, and will be disconcerted by Mr. Langdon-Davies' undiscriminating appetite for the supernormal in all its forms.

D. J. WEST

H. WARREN DUNHAM: **Sociological Theory and Mental Disorder,** Wayne State University Press, Detroit, 1959. pp. 298. $5.50

WARREN DUNHAM's name is familiar to every social psychiatrist as the co-author with R. E. L. FARIS, of *Mental Disorders in Urban Areas*. That pioneer study of the ecology of mental illness was almost as great a classic of its kind as John Snow's analysis of the ecology of cases of cholera in London: if one keeps a certain reservation in favour of Snow it is because he was able to advance beyond a purely ecological study, pointing to the Broad Street pump and to the South Thames Water Supply as conveyors of the disease whose occurrence he had systematically mapped. FARIS and DUNHAM showed that cases diagnosed as schizophrenics were admitted to mental hospitals at a significantly higher rate from the slums of Chicago than from the more salubrious areas, whereas this differential incidence rate was not shown for cases diagnosed as manic-depressives. These findings were elegantly demonstrated in a paper (reproduced in this book) which Dunham read before the American Sociological Society in 1936 but their interpretation has been the subject of a debate which still continues.

It is valuable to be able to read this short chapter, with its illuminating maps. There is, however, much else of interest in this collection of Dr. Dunham's papers, culled over a period of more than twenty years. Ecological studies have commanded his continuing interest—he is currently engaged in a prospective study of new cases of schizophrenia occurring in Detroit, which is designed to test a series of hypotheses about the influence of social factors on the onset and outcome of the illness.

In successive sections of this book Dr. Dunham applies himself to three principal questions: (1) Are there significant variations of the incidence of specific mental disorders over time, or in relation to locality, or to social class? (2) Is there a relationship between the personality type of a mental case before his breakdown and the type of disturbance he develops? (3) Does culture influence the incidence of mental illness? Not surprisingly, it is in answer to the first of these three questions that he writes with the greatest clarity and authority. His chapter on the methodology of sociological investigations of mental disorders is particularly instructive.

It is curious to note that although in his introduction he tells us that sociological inquiry is most likely to be fruitful in respect to neuroses, psychopathic personalities, behaviour or character disorders, and some types of senile psychosis and of schizophrenia—omitting psychosomatic disorders altogether, surely by an oversight—the bulk of this book is concerned with studies of the major functional psychoses. No doubt this is because early studies in this field were based upon cases admitted to state mental hospitals. It is only in recent years that attempts have been made to identify and count cases of minor psychiatric abnormality occurring in the general populations, and to relate their illness to their social environment. This is a much harder and more complex task, but one which may eventually prove the more rewarding.

Although it is easier to quarrel with the author's somewhat impressionistic portrayals of the pre-psychotic "social personality" of the catatonic and the paranoid schizophrenic patient, it is precisely in this section that one comes up against a vivid example of the usefulness of the sociologist's objective observation of our work. Dunham analysed a series of clinical records of these patients and made this comment:

"Most of these clinical records were built up not so much from the patient's own account of his experiences and behaviour, as from the accounts which other persons, mostly members of the patient's immediate family, gave regarding the patient. One fact which stands out in the clinical records is that, although there is a certain amount of objective data of both a psychological and a physiological nature, the final summary of the patient by the psychiatrist is usually in terms of the patient's social characteristics. The social characteristics in the record are much more numerous than the psychological and physiological characteristics. This would seem to indicate that the psychiatrist, although he may adhere to the procedure of clinical medicine, is nevertheless faced with the necessity of seeing and viewing his patient in social terms." (p. 190.)

This is a passage of which we are all likely to be reminded, as we write our daily clinical notes. If sociological research has as yet made slow progress towards elucidating the causes of mental illness, it can already claim to have thrown fresh light on the role of the psychiatrist, and the nature of his work.

MORRIS CARSTAIRS

VOL. 5 1960/6

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EXPERIMENTAL STUDY OF PROGNOSIS†*

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INTRODUCTION

IT IS the purpose of this report: (1) to document the quality and quantity of certain psychosocial parameters in the life history of patients with pulmonary tuberculosis; and (2) to evaluate their relevance to the natural history of the disease following diagnosis by predicting treatment outcome at the time of admission to the hospital on the basis of these psychosocial variables.

This experimental study of prognosis is based on the assumption that the patients' potential and capacity for responding to treatment are significantly influenced by the extent of psychosocial liabilities at the time of admission. The prediction to be validated by this investigation is that patients with few psychosocial assets will have a greater probability of treatment failure than those with many assets.

TABLE 1.—PART 1 OF BERLE INDEX

Objective data	Maximum score	No. of patients	Average score
Age up to 40	2	42	1·00
Not divorced or separated	2	42	0·79
Third generation American white gentile	2	42	0·86
High school education complete	2	42	0·86
Both parents in home until patient is 12 years old	4	42	2·88
No surgical treatment for symptoms	2	42	1·87
No previous formal psychiatric care	2	42	2·00
Steady employment	2	42	1·07
Duration of present illness less than 5 years	2	42	1·85
Total	20	42	13·18

METHOD

The predictive instrument employed for this study was the Berle Index [1]. Devised from a study of 700 patients in the New York Hospital, isolating psychological and social items attributed to improved patients, this Index enables an interviewer to estimate the amount of these favorable items present in patients.

As shown in Tables 1–3, the test is divided into three main headings: (1) objective data relating to such items in the patient's history as age, social status and past medical history (20 points); (2) factors concerning the patient's family and interpersonal relationships based on subjective appraisal by the patient of his own past history (30 points); and (3) evaluations of the patient's past performance, personality structure, and attitude toward his illness and toward stress as a factor in his

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† This study has been supported in part by the O'Donnell Psychiatric Research Fund.

illness based on the physician's appraisal of the patient's history and personality structure (40 points).

Raw scores obtained by adding the scores in each heading, are converted to percentage of points for each patient. Predictions are made on the basis of this percentage. To provide a basis for the estimation of discernible differences in the experimental subjects, the Berle range of scores for these subjects was arbitrarily divided into three groups of high, medium and low scores.

The subjects for this experimental study consisted of 41 patients originally studied in the spring of 1953. There were 25 males and 16 females, of which 34 were white and 7 were nonwhite, and who varied in age from 18 to 63. They were chosen at random by selecting every fifth consecutive previously untreated first admission to Firland Sanatorium. The only additional criteria were their ability to

TABLE 2.—PART 2 OF BERLE INDEX

Patient's interpretation	Maximum score	No. of patients	Average score
Previous health good	1	42	0·82
Some religious education	1	42	0·96
Emotional support from both parents	4	42	2·16
Congenial siblings	2	39	1·15
Emotional support from spouse	2	40	0·65
Sexual compatibility with spouse	2	39	0·67
No serious sexual problem	3	41	1·10
Spouse adequate economic provider*	2	16	1·12
Children not rejected	2	25	1·04
No housing problems	2	42	1·61
Occupational satisfaction	2	42	0·98
Congenial working conditions	2	42	1·21
Moderately adequate salary	2	41	1·17
Goal	3	42	1·49
Total	30		16·13

* Scored only for female patients.

read and write, the established diagnosis of pulmonary tuberculosis, and that they were not too critically ill on admission to Firland Sanatorium. The patients were interviewed for 1–3 hr within 2 weeks of admission and the scores were based on the information adduced.

A follow-up study was conducted on these patients 5 years from the time of their admission. Personal interviews were obtained from 36 patients; 4 patients could not be located although there was considerable information available on them from other sources; 1 patient refused the interview. To provide an estimate of the actual home environment for these patients, 25 were seen in their own residences; 3 were seen in their place of occupation; 7 were seen at their follow-up clinics; and 1 patient was interviewed at the jail.

The findings of this experimental study were compared with the findings of two concurrent retrospective studies at Firland Sanatorium: (1) a study of 669 discharged patients (a 3-year follow-up); and (2) a study of the characteristics of readmission to the sanatorium (1956–1957).*

Treatment failure was defined as unrelenting chronicity of the tuberculosis following admission, or relapse of the disease following discharge from the hospital. Relapse for the three series of patients investigated was defined as the re-occurrence of sputum positive for tuberculous organism as demonstrated by either smear or culture or both; or X-ray worsening other than temporary changes which could be explained on the basis of inter-current diseases of nontuberculous aetiology.

Complete clinical data were available for all three studies from Firland Sanatorium and included: sex, age, race, referring agencies, civil status, type of admission, diagnosis on admission, stage of disease, activity on admission, sputum on admission, nontuberculous diagnosis, collapse therapy,

* The authors are indebted to Haskell J. Weinstein, M.D., for the use of the data in the latter study.

VOL. 5 1960/6

chemotherapy prior to admission, chemotherapy initial disease, sputum prior to surgery, type of surgery, lesions, surgical complications, type of discharge, length of hospital stay, X-ray on discharge, National Tuberculosis Association (N.T.A.) Classification, sputum status on discharge, place of follow-up, X-ray at follow-up, attendance at follow-up, follow-up chemotherapy, re-hospitalization, expiration, and whether or not drugs were continued.

TABLE 3.—PART 3 OF BERLE INDEX

Physician's interpretation	Maximum score	No. of patients	Average score
Evidence from past performance: Not exaggerated sensitivity to traumatic situation Good interpersonal relationships (including sexual) Evidence that the activities, achievements, and other life experiences have afforded satisfaction	10	42	2·59
Evidence from personality structure: Moderate flexibility Minimal and short-lived hostility Capacity to face and solve personal problems Active participation in the give and take of daily affairs Moderate orderliness and reliability Good judgment and evidence of adequate discrimination regarding human values and goals	10	42	3·24
Prevailing attitudes of the patient toward illness and his problems at time of admission to clinic: Recognition of failure of present patterns of adjustment and willingness to adopt others Willingness to consider possibility that life stress, attitudes, and feeling states are relevant to the illness Confidence in physician, hospital, and its methods Capacity and willingness to assume responsibility in treatment	10	42	2·53
Extent to which a specific aspect of the life situation was a factor in precipitating the patient's illness: Extent to which this specific feature is modifiable with regard to the involved person, other persons, and circumstances	10	42	0·50
Total	40	42	8·86

VALIDATION OF PREDICTION: TUBERCULOUS DISEASE

In evaluating the validity of the Berle Index as a prognostic instrument in tuberculosis, the relationship of test scores to the outcome of treatment was examined within the perspective established by the retrospective analysis of the 669 discharged patients and the 137 readmitted patients during a 1-year period. The data adduced from these two studies indicated significant relationships between the failure and success of treatment of patients with tuberculosis and the following variables: sex, age, character and extent of disease on admission, stability of X-ray, drug therapy, surgery, nontuberculous diagnosis, alcoholism, and type of discharge. Examination of these variables with test scores and treatment failures in the predictive study, and treatment failure and readmissions in the two retrospective studies, indicated the following results.

Treatment outcome

Total Berle scores, of which 90 is maximum, for the 41 experimental subjects at time of admission to the hospital in 1953 ranged from 16 to 58 with an average of 38. Percentage scores ranged from 18 to 66 with an average of 42 per cent.

The failure to respond to treatment as evidenced by chronicity of illness or relapse was significantly related in the predictive study to low Berle scores, whereas none of the patients with medium or high Berle scores was a treatment failure. Relapse or chronic disease occurred in 5 patients or 12 per cent of the 41 patients in the predictive study, and all 5 were in the low Berle score group (Table 4). The test score for 4 of these patients was 27 points (31 per cent) and for 1 patient, 16 points (18 per cent). Of these treatment failures 2 relapsed 22 months and 52 months after initial discharge. One patient relapsed 26 months after the initial discharge and again 6 months after the second discharge. One patient was discharged after 37 months hospitalization and remained quarantined at home with highly positive sputum. The other chronic patient

TABLE 4.—RANGE OF BERLE SCORES

Points	Per cent	No. of patients*	Treatment failure
47–58	52–66	9	0
30–44	34–50	17	0
16–28	18–33	15	5 (12%)

* 41 Patients (16 Females and 25 Males).

VOL.
5
1960/6

left the hospital against medical advice after his first admission, was readmitted 22 months later, and again left against advice with sputum reported positive. Of the relapsed patients there was one tuberculous death. The patient died of massive haemoptysis which coexisted with progressive cardiac failure. A standard error of the difference was computed and the observed difference was statistically significant at the 0·05 level.

Treatment failure as evidenced by relapse in the retrospective study of 669 discharged patients occurred in 64 patients or 11·2 per cent of the original sample. Forty per cent of the relapses occurred in the first 9 months and 55 per cent occurred in the first 18 months. Of the relapsed patients there were 3 tuberculous deaths. Of the 137 patients in the one-year study of readmissions 77 patients or 56 per cent were readmitted for relapse. Readmissions were 14 per cent of the total 958 admissions for that one year at Firland Sanatorium and the readmissions with relapse were 8 per cent of total admissions.

Sex and age

Significant relationships were found between sex and age of the patients, Berle scores, treatment failure and readmission. In the predictive study all of the treatment failures were males. Ages of these patients were 40, 55, 57, 58 and 63. In this study male sex correlated significantly with low Berle score ($P < 0{\cdot}05$), older males having predominantly low Berle scores. Seventy-two per cent of the males in this study were over 40 years old and 69 per cent of these males received low Berle scores. The younger females had high Berle scores ($P < 0{\cdot}05$). Eighty-one per cent of the females in the

study were under 40 years old and 39 per cent of these females received high Berle scores (Table 5).

The relapse rate in the discharged study was 11·5 per cent for the males compared to 6·5 per cent for the females, and 14 per cent of the relapses occurred in the age group 50–59. In the study of readmitted patients, 75 per cent of the readmissions were male compared to 25 per cent who were female.

TABLE 5.—BERLE SCORES AND SEX AND AGE

Berle scores	0–39 Years		40–69 Years	
	Male	Female	Male	Female
High	1	5	2	1
Medium	2	7	7	1
Low	4	1	9	1
Treatment failure	0	0	5	0

Character and extent of disease on admission

In the predictive study there was no significant relationship between Berle scores or treatment failure and the character and extent of disease on admission (Table 6). Two of the treatment failures had far advanced disease with cavity on admission and 3 had moderately advanced disease. One of these had cavitary disease. The percentages of disease stage for patients with high Berle scores (44 per cent F.A., 33 per cent M.A., 22 per cent Min.) did not differ from the percentages of disease stage for patients with low Berle scores (40 per cent F.A., 53 per cent M.A., 7 per cent Min.), nor did the percentages of cavity for patients differ with Berle scores.

TABLE 6.—BERLE SCORES AND DISEASE STAGE

Berle scores	Far advanced	Moderately advanced	Minimal
High	4 (3)*	3 (2)	2
Medium	6 (4)	9 (3)	2
Low	6 (5)	8 (2)	1
Treatment failure	2 (2)	3 (1)	0

* Parentheses means cavity.

In the study of discharged patients treatment failure was related to the extent of original disease: 4·5 per cent of those admitted with minimal disease relapsed, 7·6 per cent of those with moderately advanced disease relapsed, and 11·8 per cent of those who had far advanced disease relapsed, a three-fold increase. The presence of cavity in the moderately and far advanced disease cases of this study increased the relapse rate approximately 1·5 per cent over the noncavitary disease of the same extent.

In the study of the readmitted patients 48 per cent had far advanced disease on the original admission compared to 41 per cent with moderately advanced and 11 per cent with minimal disease. Advanced stages of disease occurred more frequently in subsequent admissions. Thirty-one per cent of the patients for whom this was the second

admission had far advanced disease. Fifty-seven per cent of the patients for whom this was the third admission had far advanced disease, and 100 per cent of the patients for whom this was the fourth admission had far advanced disease.

Stability of X-ray

There was no significant relationship between Berle scores or treatment failure and stability of X-ray in the predictive study. Cavity was present and persisted until discharge in one chronic patient. The 3 relapsed patients had no cavity on discharge and X-ray was still improving at time of discharge. The disease was considered stable at discharge for the other chronic patient. Cavity was present and persisted in 3 patients whose Berle scores were in the lower half of the range. Three-quarters of these patients had no cavity on discharge and had improving X-rays while one-fourth had stable X-rays.

In the study of 669 discharged patients, the relapse rate was 10·5 per cent in those discharged without cavity for whom the X-ray was still improving and 7·6 per cent if the disease was stable at time of discharge.

Drug therapy, type and duration

The regimens of drug treatment showed no specific relationship to treatment failure or Berle test scores. Two of the three relapsed patients who had been on isoniazid and para-aminosalicylic acid (PAS) since hospitalization, had ceased taking drugs before they relapsed. One patient, who had received Streptomycin, isoniazid and PAS for 10 months during hospitalization and for 17 months during follow-up, changed to only Streptomycin and isoniazid 6 months before admission and was on drugs when he relapsed. One chronic patient received Streptomycin and isoniazid 37 months during hospitalization and has continued them regularly. The other chronic patient received isoniazid and PAS at two readmissions and ceased drugs when he left the hospital against medical advice. All of the patients in the experimental study received drugs. Approximately 50 per cent received isoniazid and PAS from 5 to 14 months initially, and all were discharged still on drugs. Approximately 31 per cent were still on drugs 4 years after original admission.

There was no difference in relapse rates between patients who received drugs and those who did not in the study of 669 discharged patients. Eleven and a half per cent of the patients who received isoniazid and PAS relapsed and 11·5 per cent of the 75 patients who received no drugs at all relapsed. Length of drug therapy was significantly related to relapse in this study. Every 10 months of drug therapy halved the relapse rate. Those receiving drugs 0–9 months had a relapse rate of 17 per cent while those receiving drugs 10–19 months had a relapse rate of 8 per cent. Those receiving drugs 20 months had a relapse rate of 4 per cent.

In the study of the characteristics of readmitted patients, only 63 per cent had had adequate chemotherapy during their original hospitalization.

Surgery

There was no significant relationship between Berle scores or outcome of treatment and surgery. One chronic patient had segmental resection with complications and spread of disease. There were more surgical procedures in those patients in the lower half of Berle scores. Twenty per cent of the surgery occurred in patients in the lower

VOL.
5
1960/6

half of Berle scores compared to 7 per cent in the upper half of Berle scores. Of the 12 patients who had surgery 40 per cent of these had surgical complications. Thirty per cent of the females had surgery compared to 24 per cent of the males. Only 1 female had surgical complications.

In the study of 669 discharged patients the intervention of surgery decreased the rate of relapse. The relapse rate for non-resected patients in this study was 11·3 per cent compared to 5·5 per cent in the resected group. In the surgical group where cavity was resected the relapse rate was 6·9 per cent compared to 5 per cent in whom non-cavity disease was resected.

Most of the surgery for the readmitted patient group had occurred during their original hospitalization. Twenty-nine of these patients or 22 per cent had had resectional surgery during their first admission, and 10 patients or 9 per cent of those for whom this was the second admission had surgery during this readmission. None of the patients for whom this was the third or fourth admission had tuberculous surgery in this readmission.

TABLE 7.—BERLE SCORES AND NONTUBERCULOUS ILLNESS

Berle scores	Other illness	Alcoholism	Against medical advice	No. of patients
High	1 (11%)	0	1 (11%)	9
Medium	7 (41%)	2 (12%)	2 (12%)	17
Low	14 (93%)	11 (73%)	6 (40%)	15
Treatment failure	4	4	2	5

Nontuberculous diagnosis

In the predictive study the diagnosis of a secondary nontuberculous illness correlated significantly ($P < 0{\cdot}01$) with low Berle scores (Table 7). Although 4 of the 5 treatment failures had the following nontuberculous diagnoses: (1) emphysema, benign prostatic hypertrophy, hernia, obesity; (2) emphysema; (3) hernia, laparectomy; (4) possibility of Addison's disease, secondary diagnoses occurred in such frequency in the entire study group that there was not a significant relationship between treatment failure and secondary diagnosis. Thirty-four per cent of the patients in the study had nontuberculous illness, and 93 per cent of those with low Berle scores had nontuberculous illness. Types of illness included: anemia, emphysema, psoriasis, peptic ulcer, psychosis, and carcinoma of the skin. There were 42 nontuberculous deaths or 6 per cent in the study of discharged patients. Cause of death was evenly distributed between cancer and heart and vascular disease.

In the study of readmissions, the incidence of nontuberculous illness and nontuberculous deaths increased with subsequent admissions. Twenty-one of the 137 patients or 15 per cent had had a psychiatric diagnosis on their original admission and 17 of the 110 or 15 per cent of those for whom it was the second admission had a psychiatric diagnosis during this readmission. In this study 5 patients or 4 per cent of those for whom this was the second admission died of nontuberculous illness. Deaths were attributed to carcinoma of the larynx, congestive heart failure, carcinoma of the pancreas, carcinoma of the lung, and a squamous cell carcinoma of the skin. Three patients or 14 per cent for whom this was the third admission died of nontuberculous

illness which included adenocarcinoma, carcinoma of the larynx, and massive hemoptysis. Seventy-five per cent of the nontuberculous deaths in this study were attributed to carcinoma. Patients for whom this was the fourth admission had nontuberculous diagnoses of empyema, bronchopneumonia and severe pulmonary insufficiency.

Alcoholism

There was a very significant ($P < 0{\cdot}01$) relationship between Berle scores, treatment failure, and alcoholism (Table 7). Four of the 5 treatment failures were alcoholics. Thirty-two per cent of the experimental group were alcoholics and 73 per cent of those receiving low Berle scores were alcoholics. Of the 13 alcoholics in the study, only one was a female [2–4].

In the retrospective study of discharged patients, 108 or 16 per cent of the original sample had a diagnosis of alcoholism and relapse occurred in 23 per cent of these.

Alcoholism or questionable alcoholism was diagnosed in one-third of the readmitted patients in their original hospitalization. This rate was higher for patients for whom this was the second admission (45 per cent), and still higher (59 per cent) for patients for whom this was the third admission.

Type of discharge

Discharge from the hospital against medical advice or being absent without leave correlated significantly ($P < 0{\cdot}01$) with treatment failure and low Berle scores (Table 7). Two of the patients who were treatment failures had been discharged against medical advice. Nine or 22 per cent of the experimental study group left the hospital against advice and 40 per cent of those with low Berle scores left against advice.

In the study of 669 discharged patients, those discharged with medical advice relapsed one-fourth as often as patients who left against advice. Relapse occurred at a rate of 7·2 per cent for those discharged with advice compared to 27·4 per cent for those discharged against advice.

In the study of readmitted patients in a one-year period, 36 per cent had been discharged previously against medical advice. In addition, one-fifth of the readmitted patients had been interned on the locked ward as disciplinary problems during their previous hospitalizations.

VALIDATION OF PREDICTION: PSYCHOSOCIAL ADJUSTMENT

An analysis of original Berle Indices indicated that this tuberculous patient group had few psychosocial assets. Scores of this group were considerably lower than those obtained by Berle [1] and by Wolff and Wolf [5] in applying the scale to patients with asthma, migraine headache and hypertension where a score of below 60 per cent was associated with failure to improve, scores between 65 and 75 per cent with symptomatic improvement (slight to major change in symptoms, basic attitudes and stress reactions), and scores greater than 80 per cent with basic improvement. Ninety-eight per cent of this tuberculous group had scores less than 60 per cent (Table 8).

Scores for this patient group were particularly low in those items of the test which indicated minority group status, divorce, marital discord, incomplete education and job dissatisfaction, and in the area of modifiability of life stress. The low scores in this latter section indicated that in addition to illness being precipitated by an acute life

VOL.
5
1960/6

crisis, these patients suffered from long term social liabilities which needed little in the way of crisis to instigate disease.

Replication of Berle scores

A replication of the Berle test 5 years after the original hospitalization showed that the capacity for change and improvement in adjustment was significantly influenced by

TABLE 8.—COMPARISON OF OTHER STRESS DISEASE RESULTS AND THIS TUBERCULOSIS STUDY

	Other stress diseases	Tuberculosis study group
I	Over 80%	52–66%
II	65–75%	34–50%
III	Under 65%	18–33%

the amount of psychosocial liabilities. Thirty-five patients or 85 per cent of the patient group had scores within 6 points of the original tests, and were, therefore in the same Berle percentage group (Table 9).

Although the estimation of assets in the second Berle test was made on the basis of the patient's adjustment and satisfaction in the period since hospitalization, the results were the same as those based on his entire life adjustment at admission. The low scored items in the original Berle were equally low in the second Berle test. Patients lost additional points in the second Berle for "age up to forty years," "surgical treatment for symptoms," and "duration of illness less than five years."

TABLE 9.—REPLICATION OF BERLE SCORES

		1958		
		High 52–66%	Medium 34–50%	Low 18–33%
1953	High	100	—	—
	Medium	12	82	6
	Low	—	20	80

The following case demonstrates the technique for scoring each patient at the time of hospitalization and follow-up, and the similarity of psychosocial assets and performance at two instances.

This patient was a 29-year-old Negro female who was born to older, intensely religious, rigid Protestant parents, and who grew up in the segregated society of a small Louisiana town. The patient was the youngest of 3 children and described herself as "a real good girl" who had a "happy childhood." Early in life she showed evidence of rather marked dependency on her parents. She did not graduate from high school because her mother became ill with arthritis and menopausal difficulties, and the patient remained home to care for her.

In 1944, at the age of 20, the patient went to Los Angeles to live with relatives and work in a defense plant. She spoke with a fair degree of animation of the life in Los Angeles, but she remained only 5½ months because her mother was again in poor health. After a few months, with improvement in her mother's health, she went to Kansas City. She worked in a factory there but stated that she

was afraid the entire time in Kansas City because of the gangsters about whom she had heard so much. She again returned home at the request of her mother.

At this point in her life, the man she later married returned from war service to the small town in Louisiana, and after a month of superficial acquaintanceship, they were married. The marital adjustment was always poor. As she phrased it, "My kids come first. I don't drink and I don't smoke. I feel odd when I go out with him; I feel fine if he goes out without me." She spoke of herself as "not a hot-blooded woman" who preferred church activities. Her husband preferred sports and parties. She resented the fact that he was not a good provider and stated, "My father built a home for my mother. Here we are packed in; I need my own home." The husband chose Seattle as a place to live, and in 1946 they moved here. The choice was on the basis of his mother's preference. The patient always resented the separation from her family and stated, "I always keep the fare home available."

It was in this setting of unfulfilled dependency needs, and an increasingly strained marital adjustment in a new and unsympathetic environment, that the patient developed pulmonary tuberculosis. The patient went on to state, "I don't think I've grown up; I still keep thinking of those free days. I worry about my family because I didn't go home. I guess I'm all mixed up. I think I worry more about things that might happen than things that are." The patient concluded with a request for psychiatric help.

Five years after admission, this patient was interviewed in her own home and in her physician's office. The patient was cooperative and friendly. The home, a deteriorated wood structure in a low income non-white neighborhood, was adequate in size for the patient and her two children. The interior was furnished with inexpensive, worn furnishings but was very orderly and clean.

This female was discharged with advice 9 months after admission. Her disease status on discharge was: inactive, improved without cavity. Her sputum was negative by concentrate and culture. She had had no surgery nor secondary illness. Her disease on admission was minimal without cavity.

Several months after discharge, the patient learned of her husband's infidelity during and after her hospitalization. She separated from him and said, "I could never forgive him." In order to make payments on her house and to assume responsibility for her husband's debts, the patient worked as a waitress in a department store. At this time she was pregnant. She was followed by an internist in the early months of pregnancy and suffered from hyperemesis gravidarum, aborting the child.

The patient's main preoccupation at this time was with her two school age children. She mentioned that she felt they blamed her for the divorce and that when her former husband come to visit them, he told the children that their mother would not have him back. Their attitude influenced her feelings about dates as well, and she seldom saw men for this reason. The children themselves were active in school and had the friends and interests of most children their age. Her husband visited occasionally and she said, "I could never take him back—even though the Bible says to forgive; I guess I still love him deep down."

Since her hospitalization, the patient has made four trips to Louisiana to visit her 94-year-old father and 64-year-old mother. She talked of moving to Louisiana but felt the segregation problem would be too great for her children, and said, "Here, they don't know the difference."

In the fifth year after discharge, the patient quit her job. She stated she wanted to spend more time with her children. At this time she was receiving ample support from her husband and had accumulated savings; she was receiving unemployment compensation on the basis of being employable.

Spending the entire day in the home, the patient described her daily routine of housework and television as "lonely and lazy." She said, "I know I should get out more and see people—it's my own fault." Her lack of social participation or interest was directly related to her rigid and Puritanical background since she felt most groups would be "gossipy," and her neighbors were prone to "drinking beer and use of profanity." Her one pleasure was to attend movies but again she was afraid of "the men who come and sit by you in the theatre or come up to you at the bus stop."

With the exception of the pregnancy, occasional colds and constipation, the patient remained well after her discharge. She spoke of "sleepless nights," stating, "I worry all the time." She was seen by two gynecologists. Her dependency was apparent in her attempt to please and be advised by all authoritative figures. She was cooperative in the hospital and followed her outpatient regime zealously, as well as seeing three separate physicians for care and consultation. She was particularly receptive to the internist who had originally interviewed her for a Berle score and had followed the

VOL.
5
1960/6

case thereafter. She expressed her own awareness of her dependency by stating, "I always had someone to care for me; I know now I have to grow up and be my own boss."

In attempting to assume the responsibilities of adulthood, this patient adequately supported her children, was reliable about her employment while working, and maintained an orderly and well-regulated home. She was conscientious in her striving to provide honest and realistic goals as well as encouragement and support for her children. She was dispassionate regarding her status as a Negro.

This patient received 49 out of a possible 90 points or 54 per cent in her original Berle scoring, placing her relatively in the highest third of all the Berle scores. In the follow-up, the patient received 46 points or 51 per cent.

The evidence from two interviews with the patient in 1958 showed that there was relatively little difference in the patient's performance and adjustment since 1953. The evidence in the second interview indicated that her dependency and immaturity still interfered with her attempts at adjustment. However, she had some insight into the nature of her difficulty. She persisted in aspiring for self-sufficiency and independence but remained lonely and indecisive.

The original summary in 1953 suggested that this patient had the capacity for change under therapy. After discharge from the hospital this patient did receive short term nondirective therapy wherein she was given the opportunity to discuss significant issues and problems and to receive support and advice. Willing as she was, the inherent liabilities of an overly protected childhood combined with intellectual limitations and membership in a minority racial group made this patient incapable of major change. The evidence that she had previously shown a capacity for responsibility and was continuing to show this capacity suggested that her assets were sufficient to sustain her current level of performance.

TABLE 10.—BERLE SCORES AND MARITAL STATUS

	High	Medium	Low
1st marriage, unbroken	67%	41%	13%
1st marriage, divorced	11%	12%	40%
1st marriage, widowed		6%	
2nd marriage, 1 divorce	22%	29%	7%
2nd marriage, 2 divorces		12%	13%
Single			27%

Berle scores and subsequent life adjustment

A description of life-time adjustment patterns at the time of follow-up in 1958 showed a correlation between treatment failure, predictive scores, and the level of social adjustment. The relationship of marital stability, residential and occupational status and mobility, recreational and social participation, and follow-up attendance at clinic with the predictive scores was evaluated.

Marital stability. The marital experience of patients with treatment failure and low Berle scores was extremely poor. Four of the 5 treatment failures were no longer with the original spouse. Two relapsed patients were married for 24 and 27 years and stated the marriages were always difficult. One relapsed patient was married 10 years and remarried for another 6 years. One chronic patient who was discharged with medical advice was single until age 43 when he married a 55-year-old nurse's aid from the sanatorium. The other chronic patient was married 10 years and then divorced, and stated that the marriage had always been on the verge of breaking up (Table 10).

The percentage of divorces for patients with low Berle scores was twice that of patients with high scores. Sixty per cent of the patients with low Berle scores had been divorced. Of these, 20 per cent had been remarried and 13 per cent were divorced again. Fifty-three per cent of the patients with medium Berle scores were divorced. Of these,

41 per cent were remarried and 12 per cent were divorced twice. Thirty-three per cent of the patients with high Berle scores were divorced and 22 per cent were remarried. None was divorced more than once. The percentage of patients who remained with original spouses was 13 per cent for the low Berle score patients, 41 per cent for the medium Berle scores, and 67 per cent for the patients with high Berle scores. The only patients who had decided to remain single, or patients who had not yet married, were those with low Berle scores of which there were 27 per cent.

The characteristics of the family constellation were similarly related to treatment failure and predictive scores. None of the treatment failures had had children in their homes or had kept in contact with their families in the 2 years prior to their admission. Two of the relapsed or chronic patients had had children at one time in the home and the other 3 had never had children and did not want to have any. None of the patients with low Berle scores had children in the home and 50 per cent of those who had been married had never had children. Only 2 patients in this group kept in any contact with their children. By contrast, 89 per cent of the patients with high Berle scores and 47 per cent of the patients with medium Berle scores had children in the home or were in close contact with their children.

Residency. Considering the type of residency as evidence of comfort and well-being, the patients who were treatment failures or had low predictive scores lived in marginal quarters. All of the treatment failures were living in one-room apartments, hotels on the Skid Row, boxcars or flop-houses, or missions. Three-quarters of the patients with low Berle scores lived in equally marginal residences. Fifty per cent of the patients with medium Berle scores had attractive homes and apartments, and 8 of the 9 patients with high Berle scores lived in attractive, well-kept homes with gardens.

Occupational status and mobility. The ability to attain a responsible position and to remain in one occupation which provided satisfaction and adequate income was strikingly lacking in patients with treatment failure and low predictive scores. In the 10 years prior to admission, all of the treatment failures were at one time unemployed and all had received income from public assistance or welfare agencies. For these patients job status, the duration of time on a job, and the income from the work were marginal. Types of transient occupation included night watchman, fruit picking, lawn mowing, dishwashing, logging, and construction.

Twelve of the 15 patients with low Berle scores or 80 per cent were transient, unskilled laborers who had worked on logging operations, railroad crews, and as cooks, garbage collectors and janitors. Their record of unemployment was out of all proportion to the other groups. None felt satisfaction in their positions or their income and stated their reasons for working were strictly practical. Of this group there were 25 contacts with welfare agencies (Table 11).

The employed patients with high Berle scores were all employed as skilled craftsmen or in responsible factory or construction positions or clerical work. These patients had had steady work records and expressed relative satisfaction with their job status and income. Only two contacts had ever been made with welfare agencies. Males with medium Berle scores were less satisfied. Half of these patients had responsible positions in skilled crafts, construction or sales, and the other half were casual or unskilled workers. Of the males who worked, one-third had remained on the same job 10 years and were relatively satisfied with it. Ten contacts with welfare agencies were made by these patients.

VOL.
5
1960/6

Recreation and social participation. Recreational outlets and social participation were nonconventional in patients with treatment failure and low predictive scores. The 4 alcoholic treatment failures began drinking in their forties and fifties and steadily deteriorated. All had been fired frequently for drinking and had been jailed. Three of these alcoholics did all their drinking with other mates in taverns or boxcars, while one who had few friends drank alone. The one nonalcoholic had little social life and few friends aside from contacts with his married daughters. With the exception of the quarantined chronic patient, all of the treatment failures returned to former drinking and social patterns after original discharge.

TABLE 11.—BERLE SCORES AND CONTACTS WITH PUBLIC AGENCIES

Berle scores	Number of patients	Number of contacts
High	9	4
Medium	17	10
Low	15	25

None of the patients with low Berle scores had allegiance to organizations. With the exception of 2 males under 30 years old, these patients had few friends or acquaintances. Two-thirds of these patients were lonely and transient alcoholics. By contrast, patients with high Berle scores were active in churches, clubs and unions. They had hobbies and enjoyed attending social gatherings. Although some of the patients with the medium Berle scores attended church and were active in organizations and enjoyed sports, most of them found their sole recreation in watching television or reading, and social participation was limited to family or close friends.

Follow-up attendance. Failure to attend follow-up clinic and comply with physicians' instructions was apparent in both the treatment failures and patients with low Berle scores. Although only one chronic patient was lost to the follow-up clinic, the attendance of the other patients was sporadic and unreliable, and 2 of these patients ceased drugs without permission. Sixty per cent of the patients with low Berle scores were lost to follow-up compared to 29 per cent of the patients with medium scores and 33 per cent of the patients with high scores. The patients with high scores did not attend clinics due to pregnancy or travel.

Berle scores and personality structure and attitude

The manner in which patients faced everyday life problems and the degree of appropriate understanding of what is required by social convention were demonstrably relative to predictive scores. Patients who were treatment failures or had low Berle scores were rigid, hostile and suspicious. These patients saw no relationship between their patterns of behavior and their own problems, and justified their alcoholism, unemployment and unsatisfactory interpersonal relationships as evidence of the inequities of life and of their personal mistreatment.

The conflicts of minority status, dependency and sex roles were more apparent in patients with low predictive scores. Nonwhites with low Berle scores showed overly sensitive reactions to minority status while nonwhite patients with high scores recognized and dealt with the problems of race more realistically. The problems of parental

dependency and self-assertiveness increased in the lower portion of Berle scores. All of the females with low Berle scores exhibited a close relationship and dependence on their parents. The acceptance of sex roles was particularly difficult for the patients with low scores. All the males who had never married had low scores. Female patients with low scores attempted to resolve problems in sex roles by divorce and new marriage with little success, whereas many of the females with high scores achieved some comfort and productivity via full time jobs or other outside interests.

An estimate of the eventual outcome of patients' present adjustment patterns suggested that many of the patients with low predictive scores were utilizing unrealistic adjustment mechanisms which would lead to eventual breakdown. The patterns of transient alcoholism and social isolation among the males in the low predictive group had already led to their deterioration and there was little possibility for re-establishment of productive systems in these patients. Many of the patients who had medium Berle scores were currently productive. However, their attitudes, values and methods for achieving satisfaction and comfort were so unrealistic that they could be expected to become disorganized in the face of critical life situations. A number of patients with low Berle scores were in extremely dependent circumstances at the present time, requiring considerable support from persons close to them. Since the past experience of many of these patients indicated a lack of capacity for maintaining such interpersonal relationships, their adjustment appeared precarious.

All of the patients with high Berle scores demonstrated an ability to assume responsibility and to make permanent commitments. Their methods of adjustment were based on a more realistic appraisal of their limitations and assets and appeared adequate to sustain them at present productive levels.

VOL.
5
1960/6

FORMULATION

The premises upon which this research is based are derived primarily from the province of the behavioral sciences. The relationship between outcome of treatment of an infectious disease and psychosocial variables demonstrated in this research emphasizes the importance of the behavioral sciences as basic medical sciences. The following formulation provides a universe of discourse for defining the relevance of the behavioral sciences to the science of medicine.

The science of medicine is concerned with the facts and verifiable general laws pertaining to the natural history of man in health and disease. Health may be defined as a state of well-being, of being hale, sound or whole physically, psychologically and socially. With regard to health, medical science is concerned with the qualitative and quantitative aspects of explicit and implicit behavior which are responsible for man's well-being: genetics; constitution; growth and development; maturation; aging; function, both particular and whole and including the disciplines of anatomy, physiology, biochemistry and psychology; physical environment, including the disciplines of biophysics, geography, climatology, etc.; and the socio-cultural environment which includes the disciplines of sociology, social psychology and anthropology.

During the course of his daily life man is constantly encountering situations which induce a change from the steady state and require adaptive responses to restore the equilibrium between the internal milieu of the body and the body's internal and external environment. Such reactions to the problems of daily living usually are manifested as alterations in behavior which may vary widely in degree, content, duration and effectiveness. The adequacy of man's performance in dealing with problems of adaptation is determined by the relevance and pertinence of the action taken, the timing of the action, and the reason or motivation for the action taken to resolve the difficulty. Performance or the execution in action of functions man expects of himself or which are expected of him by social convention,

which is conducive to productivity, comfort and satisfaction, has the highest probability of restoring altered homeostasis and hence is consonant with resistance and the maintenance of health.

With regard to disease processes, the science of medicine addresses itself to four specific areas: (1) the disruptive forces which can alter man's state of well-being; (2) the mechanisms by which these disruptive forces evoke bodily reactions; (3) the physical, chemical, emotional and social consequences of these reactions to disruptive forces or the genesis of disease; and (4) the processes which modify or influence these reactions of disease once they occur.

Previous studies from this laboratory have demonstrated the role of psychosocial and psychophysiologic factors in the aetiology of pulmonary tuberculosis [6–10]. These observations indicated that it was in a setting of increased life stress acting on individuals whose limited capacities were no longer adequate for resolving problems or achieving satisfaction that tuberculosis developed. Studies of 17-ketosteroid excretion indicated that adrenocortical activity plays a role in resistance to tuberculosis and that the effects of life stress upon the natural history of the disease, in part, may be mediated via the adrenal gland.

This study is primarily concerned with an evaluation of the processes which modify or influence the course of the disease once it has developed. Here, cognizance has been taken of the interrelationship of the natural history of disease and the physiologic, psychologic and sociologic disciplines.

The results of this prognostic study based on an evaluation at admission of the psychosocial parameters in the life history of patients with pulmonary tuberculosis were compared with the results of a 3-year follow-up study of discharged patients and a one-year study of readmitted patients. Treatment failure in the prognostic study was significantly related to low predictive scores.

A variety of factors was found to be equally operative in treatment failures in all three studies. The variables of male sex, old age, nontuberculous illness, alcoholism, and discharge against medical advice were significantly related to low scores and treatment failures in the predictive study, to relapse in the study of 669 discharged patients, and to the readmitted patients in a one-year period. These factors were significantly absent in patients in the predictive study who had high scores and no treatment failures, and to non-relapse patients in the study of 669 discharged patients.

Although both retrospective studies found a relationship between treatment failure and disease stage, this factor was not related to predictive scores. Surgery was not significantly related to low scores or treatment failure in the predictive study although surgery occurred twice as often in patients whose scores were in the lower half of the range of Berle scores and post-operative complications occurred four times as frequently. Surgical intervention was related to non-relapse in the study of discharged patients.

There was no significant relationship between type of drug therapy and duration of drugs in the predictive study although the highest proportion of patients who had not been seen in the follow-up clinic for over a year were those who had low Berle scores, and it is a reasonable assumption that they had ceased taking their drugs. Prolonged drug therapy was significantly related to non-relapse in the study of discharged patients.

Other follow-up studies [11–15] of discharged tuberculous and nontuberculous patients showed a relationship between many of these same variables and treatment outcome.

A comparison of the original Berle scores with the scores at the time of follow-up indicated that all but 6 patients had the same degree of psychosocial assets. The same low scores were found in specific items of the test in 1953 and 1958. A comparison of the marital, occupational, and recreational participation and satisfaction demonstrated the patients who were treatment failures or had low predictive scores were unable to perform with comfort and satisfaction in any of these areas. Most of these patients were transient, lonely and aimless males who had little in the way of social ties or primary group relationships. By contrast, the patients with high scores were currently married, had job tenure, adequate income, and outside interests and activities.

A comparison of the personality structure and attitudes of patients demonstrated that patients with low scores were rigid, hostile and suspicious, and they had more conflicts in accepting minority status, dependency, and sex roles. These patients felt they had been deprived and mistreated, and saw no relationship between their patterns of behavior and their own problems. These characteristics were particularly apparent in the treatment failures.

An estimate of the eventual outcome of the patients' present adjustment patterns suggested that many with low predictive scores were utilizing unrealistic adjustive mechanisms which could lead to eventual relapse of disease and that patients with high scores were utilizing more realistic methods capable of sustaining present performance levels.

These data indicate that the significant parameters which modify or influence the course of pulmonary tuberculosis once it occurs include: (1) new aetiologic agents which include the presence of the disease itself; (2) biologic endowment; (3) past conditioning experiences and patterns of adaptive behavior; and (4) new conditioning experiences. In addition to the doctor's role in management of the patient, it is obvious that the qualitative and quantitative aspects of patient's primary group relationships, social class, ethnic status and sex role are of paramount importance in determining the content of the new conditioning experiences and hence treatment outcome.

In essence, it can be adduced from the data in this study that man's concept of himself and his conformance with what is expected of him result in large part from the cultural milieu in which he lives. The evolution of attitudes, values, aspirations and techniques for achieving goals which approximate the cultural norms is essential to homeostasis, productivity and satisfaction. The success of this process of cultural conditioning depends in part on the nature of the individual, the nature of the social pressures encountered, and the effectiveness of the methods available for dealing with them. Individuals who are liberally endowed with assets can usually define their status with relative ease. For such individuals the possibility for conflict and anxiety is minimized and the techniques for resolving tensions are reasonably effective. By contrast, individuals with relatively few assets often experience considerable difficulty in finding their place and making accurate discriminations concerning what is and what is not dangerous. The possibility for conflict and anxiety abounds, and the techniques utilized for dealing with ensuing difficulties are often irrelevant, impertinent and ineffectual.

The greater the assets, the higher the probability that the individual will be equipped with knowledge concerning the availability and applicability of those methods of living which are most conducive to the maintenance of homeostasis and enhanced resistance to disease. The fewer the assets, the higher the probability that the

VOL.
5
1960/6

methods of living utilized will lead, as a by-product, to seriously disrupted homeostasis and lowered resistance to disease and permit the emergence of a condition or state in which the physical, emotional and social aspects of health are significantly altered. Impaired performance or capacity for productivity, deviant behavior, then, becomes the cardinal sign of disease; discomfort and dissatisfaction the cardinal symptoms. The disability which ensues is relative, being dependent on the degree to which the liabilities outweigh the assets.

SUMMARY

An experimental study was conducted to evaluate the relationship between psychosocial assets and treatment failure or success in tuberculosis. It was suggested that patients with the least amount of psychosocial assets would have a greater probability of treatment failure.

The instrument used to measure assets was the Berle Index. Patients were interviewed and scored at the time of their hospital admission and the results of this study were compared with a follow-up study on the same patients 5 years after hospital admission, and with a 3-year follow-up of 669 discharged patients and a one-year study of 137 readmitted patients.

A comparison of the results of the three studies showed that patients in the predictive study who showed treatment failure were those who had low predictive scores, and that characteristics of these treatment failures and of patients with low predictive scores were related to the characteristics of both relapsed and readmitted patients. These characteristics of male sex, alcoholism, nontuberculous illness and against medical advice discharge found in the treatment failures of all three studies were significantly lacking in those patients with high Berle scores.

An estimate of change in the degree of psychosocial assets in the patients in the predictive study was made by a comparison of the original Berle scores with scores at the time of follow-up. It was shown that patients had the same amount of psychosocial assets at the time of the repeat study and that performance was identical. Adjustment patterns for patients with low Berle scores, and particularly for those who were treatment failures, were inadequate, non-integrated and conducive to eventual breakdown. By contrast, the patients with high scores were able to achieve comfort and satisfaction in their present levels of adjustment.

There was a striking validation of the hypothesis that the quality and quantity of psychosocial assets provide a basis for making a prognosis.

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VOL.
5
1960/6

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THE RELATION OF SERUM ASCORBIC ACID LEVEL TO ADRENOCORTICAL SECRETION DURING EXPERIMENTALLY INDUCED EMOTIONAL STRESS IN HUMAN SUBJECTS*

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OL.
5
0/61

INTRODUCTION

THE secretion of hydrocortisone by the adrenal cortex is frequently associated with a reduction in the ascorbic acid content of the gland [20] and with an increase in the concentration of this vitamin in the blood [2, 22]. The precise nature of this mechanism is unknown, although considerable speculation concerning it occurs in the literature [22]. During the course of a study of the effect of an experimental psychological stress on a variety of biochemical variables, we were able to measure simultaneously the levels of hydrocortisone and ascorbic acid in plasma samples obtained prior to, during, and after the application of the stress stimulus. The relationships which were obtained between the two variables suggested that the serum level of ascorbic acid might be an important determinant of the quantity of hydrocortisone secreted by the adrenal cortex following the application of the stress stimulus. We consequently varied the concentration of ascorbic acid in the serum in order to test this assumption directly. The present paper is a report of the degree of relationship found to occur between the levels of serum ascorbic acid and plasma hydrocortisone simultaneously measured before, during, and after an experimental stress, and of the effect of varying the serum ascorbic acid level on these relationships.

SUBJECTS, EXPERIMENTAL DESIGN, AND METHODS

The subjects, experimental design, and methods of the first experiment of this study have been described in detail in a previous publication [11]. Briefly summarized, blood samples for the determination of plasma hydrocortisone and serum ascorbic acid were drawn from a group of twelve healthy volunteers (college students) before, during, and after an experimental, psychological stress. The stress consisted of an anxiety state induced while the subjects were in a hypnotic trance. Anxiety states have been previously shown to produce an elevation in the plasma level of hydrocortisone [10, 12, 13]. The subjects had been previously trained to achieve a hypnotic trance during which an anxiety state could be induced and subsequently abolished with no recall of the total experiment on their part. Four distinct, contiguous, experimental occasions were obtained: (1) a prehypnotic, waking state; (2) a period

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of basal hypnosis; (3) a hypnotically-induced anxiety state, and (4) a post-hypnotic, waking state.

In order to determine the effect of varying the serum level of ascorbic acid on the plasma hydrocortisone response to the anxiety-stimulus, a second experiment was carried out. Five of the original 12 subjects were given 500 mg ascorbic acid daily for seven days prior to the test day. On that day, the hypnotic induction, establishment of the anxiety state, and termination with total amnesia for the procedure were repeated.

Quantitative estimates of the intensity of the experimental stress were derived from changes in performance across occasions on several standard psychological tests. The Rorschach test was employed as a measuring instrument in the first experiment [7], and the Taylor Manifest Anxiety Scale and the Barron Ego-Strength Scale were used in the second [4].

Hydrocortisone was determined by Nelson and Samuel's method [9, 3]. Ascorbic acid was measured by the method of Mindlin and Butler [8].

RESULTS

Relation of serum ascorbic acid level to plasma hydrocortisone level

The mean serum ascorbic acid and plasma hydrocortisone levels of the 12 subjects on the four occasions of testing in the first experiment are given in Table 1. Analysis of

TABLE 1.—SERUM ASCORBIC ACID AND PLASMA HYDROCORTISONE LEVELS OF TWELVE SUBJECTS ON FOUR OCCASIONS OF TESTING*

Occasion	Serum ascorbic acid (mg %)			Plasma hydrocortisone (μg %)		
	Males	Females	All Ss	Males	Females	All Ss
Pre-hypnosis	1·39 ± 0·97	2·70 ± 0·70	2·05 ± 1·06	22·5 ± 4·7	19·3 ± 8·1	20·9 ± 6·5
Hypnosis	1·24 ± 0·88	2·53 ± 0·67	1·89 ± 1·01	13·2 ± 7·3	12·5 ± 3·8	12·9 ± 5·5
Hypnosis + anxiety	1·28 ± 0·76	2·67 ± 0·66	1·98 ± 0·99	12·1 ± 5·9	20·2 ± 4·7	16·2 ± 6·6
Post-hypnosis	1·29 ± 0·72	2·60 ± 0·48	1·95 ± 0·90	10·4 ± 7·9	12·9 ± 6·0	11·7 ± 6·8

* Means ± standard deviations: six males and six females.

variance among the serum ascorbic acid levels by sexes and occasions indicates a significant difference in level between female and male subjects, and no significant difference in level among the four testing occasions (Table 2). The female subjects exhibited a serum ascorbic acid level about twice that of the male subjects on every occasion of testing. The level of the male subjects is that of a healthy, well-nourished population and is about the same as previously reported levels [19]; the female group's level is greater than the value reported for any previous group [1]. The female subjects of this study were in a position to select and actually did select a diet extremely high in vitamin C content. A similar analysis of variance among the plasma hydrocortisone levels gives diametrically opposite results: no significant difference between the sexes but a significant difference in level among the four occasions of testing. When these results are viewed in the light of the known diurnal trend in plasma hydrocortisone level, other analyses are suggested which better evaluate the

data [11]. In the paper cited, a comparison of the changes in hydrocortisone level between adjacent occasions indicated that the *increase* in hydrocortisone level following the application of the hypnotically-induced anxiety state was greater for the female subjects than for the males, who actually showed a *decrease* on the average.

The preceding findings suggested that the elevation in plasma hydrocortisone level following the application of the stress stimulus may be related to the level of ascorbic

TABLE 2.—ANALYSIS OF VARIANCE AMONG SERUM ASCORBIC ACID LEVELS BY SEXES AND OCCASIONS

Source of variation	*df*	MSq.	*F*
Between sexes	1	21·081	10·44†
Between subjects within sexes	10	2·020	
Between occasions within males*	3	0·026	0·28
Occasions × subjects within males	15	0·095	
Between occasions within females*	3	0·033	1·09
Occasions × subjects within females	15	0·030	
Total	47		

ANALYSIS OF VARIANCE AMONG PLASMA HYDROCORTISONE LEVELS BY SEXES AND OCCASIONS

Source of variation	*df*	MSq.	*F*
Between sexes	1	34·003	0·48
Between subjects within sexes	10	69·948	
Between occasions	3	203·427	7·22‡
Occasions × sexes	3	71·775	2·55
Occasions × subjects within sexes	30	28·184	
Total	47		

* Since the occasion × subject variances are significantly different in the two sexes, it is necessary to test the difference between occasions separately within each sex.
† Significant at better than the 0·01 level.
‡ Significance at better than the 0·001 level.

acid in the serum. In order to test this hypothesis, a number of correlation coefficients between these two variables were determined. Intercorrelations of the individual levels on identical occasions are given in the first four rows of Table 3. On the third occasion (hypnosis + anxiety), the correlation coefficient is highly significant, a finding due to a real increase in covariance rather than to an apparent increase resulting from alteration in variance since the variances were found not to change significantly from occasion to occasion [25].

Since the individual ascorbic acid and hydrocortisone levels maintain their positions relative to the group across all occasions (coefficient of concordance, *W*, for

ascorbic acid = 0·90; $df = 11$; $P < 0{\cdot}001$; W for hydrocortisone in females = 0·71; $df = 5$; $P < 0{\cdot}01$; W for hydrocortisone in males = 0·20, $df = 5$; P, N.S.), we consequently assumed that the hydrocortisone levels during the anxiety occasion were significantly related to the ascorbic acid levels on the other three occasions. The fifth to seventh rows of Table 3 indicate that this assumption is true. Also, the increase in hydrocortisone level following the anxiety stimulus (occasion 3 minus occasion 2) and the decrease in level following the termination of the trance (occasion 4 minus occasion 3) are significantly related to the ascorbic acid levels of the various occasions as shown in the bottom of Table 3. The lower values of these intercorrelations probably reflect the variance introduced by the hydrocortisone levels of the non-anxiety occasions.

TABLE 3.—INTERCORRELATIONS (r) OF SERUM ASCORBIC ACID LEVELS WITH PLASMA HYDROCORTISONE LEVELS AND CHANGES IN LEVEL

Occasions compared§		Correlation coefficient, (r)
Ascorbic acid	Hydrocortisone	
1	1	−0·10
2	2	0·32
3	3	0·89‡
4	4	0·24
1	3	0·82†
2	3	0·80†
4	3	0·84‡
1	3 − 2	0·56
1	4 − 3	−0·56
2	3 − 2	0·55
2	4 − 3	−0·60*
3	3 − 2	0·72†
3	4 − 3	−0·62*
4	3 − 2	0·62*
4	4 − 3	−0·55

* Significant at better than the 0·05 level;
† At better than the 0·01 level;
‡ At better than the 0·001 level.
§ The figures below refer to occasions:
1 = pre-hypnosis, 2 = hypnosis, 3 = hypnosis + anxiety, 4 = post-hypnosis.

Effect of elevating the serum ascorbic acid level on the plasma hydrocortisone response to anxiety

The high degree of correlation between the serum ascorbic acid levels on any occasion with the plasma hydrocortisone levels following the anxiety stimulus suggests that the serum ascorbic acid level may be an important determinant of the adrenal cortical response to stress. In order to test this assumption directly, a second experiment was performed in which 5 of the original 12 subjects (4 males, 1 female) were given 500 mg of ascorbic acid per day for seven days. On the eighth day, the original stress experiment was repeated with a few modifications. Each subject was

VOL.
5
1960/6

hypnotized individually but all subsequent procedures were conducted at the same time for all 5 subjects in order to expedite the experiment. No significant difference in the behaviour of the subjects from their previous day of testing was noticed.

As a more rapid index of the effectiveness of the anxiety stimulus [4], the Taylor Manifest Anxiety Scale and Barron Ego-Strength Scale were administered to each subject during each experimental occasion in place of the Rorschach test which had been similarly administered in the first experiment (Table 4). Analysis of variance among the Taylor and Barron scores indicates that the scores achieved on both tests

TABLE 4.—TAYLOR MANIFEST ANXIETY SCALE AND BARRON EGO-STRENGTH SCALE SCORES OF FIVE SUBJECTS ON FOUR OCCASIONS OF TESTING*

Occasion	Taylor scale	Barron scale
Pre-hypnosis§	10·4 ± 3·0	52·4 ± 5·2
Hypnosis	14·4 ± 4·4	43·4 ± 5·0
Hypnosis + anxiety	31·6 ± 4·8	39·6 ± 3·4
Post-hypnosis	10·6 ± 3·6	47·0 ± 4·1

ANALYSIS OF VARIANCE AMONG TAYLOR AND BARRON SCORES BY OCCASIONS

Source of variation	Taylor Scale			Barron Scale		
	df	MSq.	*F*	*df*	MSq.	*F*
Between subjects	4	36·00		4	59·95	
Between occasions**	3	506·98	52·98‡	3	148·40	21·76‡
3 vs. 1, 2, 4	(1)	1470·15	153·62‡	(1)	240·00	35·19‡
2 vs. 1, 4				(1)	132·30	19·40‡
1 vs. 4				(1)	72·90	10·69‡
Between 1, 2, 4	(2)	25·40	2·65			
Occasions × subjects	12	9·57		12	6·82	
Total	19			19		

* Means ± standard deviations.
† Significant at better than the 0·01 level;
‡ At better than the 0·001 level.
§ The pre-hypnosis values were obtained at the time of the original subject selection several weeks prior to the second experiment.
** The figures below refer to occasions: 1 = pre-hypnosis, 2 = hypnosis, 3 = hypnosis + anxiety 4 = post-hypnosis.

during the hypnosis + anxiety occasion are significantly greater and lesser respectively than on the other three occasions. The Taylor scale was particularly sensitive to the anxiety stimulus, rising to a value nearly three times greater than on any of the other three occasions. The Taylor scores obtained on the remaining three occasions did not differ significantly among themselves. The decrement in the Barron scores was not as great as the increment in the Taylor scores, amounting to about 25 per cent. The Barron scores on the three non-anxiety occasions differed significantly among themselves; the hypnosis occasion was significantly lower than during the other two

waking periods. This finding is consistent with the hypothesis that the induction of hypnosis is associated with a reduction in ego controls. The general conclusions about the psychological effects of the anxiety stress obtained in this experiment are not unlike those drawn from the Rorschach data of the first experiment.

The ascorbic acid and hydrocortisone levels obtained in the second experiment are given in Table 5 along with the comparable values for the same subjects from the first experiment.

TABLE 5.—SERUM ASCORBIC ACID AND PLASMA HYDROCORTISONE LEVELS OF FIVE SUBJECTS ON FOUR OCCASIONS IN EACH OF TWO EXPERIMENTS†

Occasion	Ascorbic acid		Hydrocortisone	
	No Vit. C (mg %)	+Vit. C (mg %)	No Vit. C (μg %)	+Vit. C (μg %)
Pre-hypnosis	1·49 ± 1·49	2·12 ± 1·07	20·8 ± 4·9	24·0 ± 11·7
Hypnosis	1·34 ± 1·42	2·10 ± 1·20	12·4 ± 7·9	17·6 ± 9·0
Hypnosis + anxiety	1·57 ± 1·42	1·84 ± 0·82	13·5 ± 9·5	21·9 ± 9·2
Post-hypnosis	1·41 ± 1·20	1·23 ± 1·06	11·9 ± 8·0	12·8 ± 6·9

ANALYSIS OF VARIANCE AMONG SERUM ASCORBIC ACID AND PLASMA HYDROCORTISONE LEVELS BY EXPERIMENTS AND OCCASIONS

Source of variation	*df*	Ascorbic acid		Hydrocortisone	
		MSq.	*F*	MSq.	*F*
Between subjects	4	10·771		113·24	
Between experiments	1	1·373	$F_e = 2·01$	194·92	$F_e = 2·30$
Experiments × subjects	4	0·683		84·90	
Between occasions	3	0·467	$F_o = 3·56$*	181·43	$F_o = 2·29$
Occasions × subjects	12	0·131		79·24	
Occasions × experiments	3	0·440	$F_{oxe} = 5·87$*	25·26	$F_{oxe} = 0·22$
Occasions × experiments × subjects	12	0·075		114·86	
Total	39				

* Significant at better than the 0·05 level.

† Means ±standard deviations; each subject received 500 mg/day of ascorbic acid for 7 days prior to testing on the +Vit. C experiment.

Analysis of variance among the serum ascorbic acid levels indicates that the average levels between the two experiments are not significantly different (F_e not sig.). However, the average trend in level across occasions is significantly different between the two experiments ($F_{oxe} = 5·87$; $P < 0·05$). This finding makes it desirable to examine the trend in average level across occasions separately in each experiment, although when averaged over both experiments there is a significant difference between

VOL. 5 1960/6

occasions ($F_o = 3{\cdot}56$; $P < 0{\cdot}05$). In order to do this, a further analysis of variance was carried out for each experiment (Table 6). In this first experiment, no significant difference in ascorbic acid levels between occasions occurs; this would indicate that the subgroup of 5 subjects are not different from their 7 additional colleagues (see Table 2). After receiving the supplement of ascorbic acid and being subjected to the procedures of the second experiment, the 5 subjects exhibit a significant decrease in average level across the four occasions of testing ($F_o'' = 5{\cdot}90$; $P < 0{\cdot}05$). The level of ascorbic acid decreases during the post-hypnotic phase to a value below that obtained in the first experiment for the same period.

A similar analysis of variance among the plasma hydrocortisone levels of the two experiments did not reveal any significant differences although a tendency is present for the plasma hydrocortisone level to increase as anticipated during the hypnosis + anxiety occasion. The 5 subjects during the first experiment have a pattern of hydrocortisone levels across occasions almost identical to that of the male subjects alone, while in the second experiment their pattern resembles the female subjects. This

TABLE 6.—ANALYSIS OF VARIANCE AMONG SERUM ASCORBIC ACID LEVELS OF FIVE SUBJECTS SEPARATELY BY EXPERIMENT

Source of variation	*df*	First experiment		Second experiment	
		MSq.	*F*	MSq.	*F*
Between subjects	4	7·500		3·955	
Between occasions	3	0·051	$F_o' = 0{\cdot}84$	0·856	$F_o'' = 5{\cdot}90$*
Occasions × subjects	12	0·061		0·145	
Total	19				

* Significant at the 0·05 level.

tendency does not achieve statistical significance, most likely because of the small number of subjects. The data suggest that the basic assumption, that an elevation of ascorbic acid level will result in a greater hydrocortisone response to a stress, is valid although the results do not achieve the confidence level which we have chosen.

DISCUSSION

It is now recognised that the regulation of the secretion of hydrocortisone is considerably more complex [24] than the simple, negative-feedback mechanism postulated a decade ago [21]. The role of ascorbic acid in the secretory process has been the subject of considerable interest. Although adrenocortical secretion can occur in the absence of adrenal ascorbic acid depletion [5, 23], enough information is presently available to link strongly the two processes and even to account for the cited exceptions. The recent work of Salomon [17, 18] has helped to explain the relation of circulating ascorbic acid to the secretory process. With the aid of ascorbic acid-1-C^{14}, Salomon has demonstrated that two forms of ascorbic acid are present in the adrenal gland; one which exchanges rapidly with the tagged material when the latter is present

in plasma and another which equilibrates much more slowly. On the basis of his studies, Salomon has suggested the following reaction sequence:

Plasma ascorbic acid $\xrightarrow{\text{fast}}$ Adrenal ascorbic acid (free) (Equation 1)

Adrenal ascorbic acid (free) $\xrightarrow{\text{slow}}$ Adrenal ascorbic acid (bound) (Equation 2)

Adrenal ascorbic acid (bound) $\xrightarrow{\text{ACTH}}$ Reaction product(s) (Equation 3)

The reaction product(s) of the last equation are most likely dehydroascorbic acid and diketogulonic acid [16, 22]. It is not known how Equation 3 influences the secretion of hydrocortisone. Since man is incapable of synthesizing ascorbic acid, the primary adrenal source of the vitamin must be plasma. The plasma level of ascorbic acid is consequently an important determinant of the adrenal ascorbic acid depletion reaction following the introduction of ACTH or the application of a stress stimulus capable of evoking ACTH release from the pituitary. It should be noted here that hypnotically-induced anxiety states are capable of significantly elevating blood ACTH levels [12, 13]. The finding that the serum level of ascorbic acid is highly correlated with the hydrocortisone level obtained during a stressful episode, coupled with the observed tendency for higher hydrocortisone levels as a consequence of a stressful experience in individuals whose ascorbic acid levels have been significantly increased, point up the complexity of the stress-induced adrenocortical secretion mechanism. They also suggest that in those situations where adrenocortical secretory enhancement is desirable, an elevated plasma ascorbic acid level may be indicated. Pincus and his coworkers [14, 15] first attempted to influence adrenocortical secretion by elevating the serum ascorbic acid level. However, after administering 100 mg of ascorbic acid daily for 13–15 days to a group of schizophrenic patients, they were unable to demonstrate an increase in urinary 17-ketosteroids or neutral reducing lipids following a test dose of ACTH. Following the administration of 4000 mg of ascorbic acid daily for four days to normal men, Kayahan [6] found that the urinary excretion of 11-oxysteroids was doubled while 17-ketosteroid excretion was reduced by a third. Apparently as daily ascorbic acid ingestion is increased from 100–500 mg to 4000 mg, a progressive change in adrenocortical reactivity occurs: no change, moderate change (but short of statistical significance), large increase. The combination of papers cited strongly support the thesis that a high serum ascorbic acid level coupled with a high daily vitamin C intake is essential to an optimal adrenocortical function. Whether raising the serum level of ascorbic acid also alters the metabolism of the adrenocortical hormone, hydrocortisone, is presently not clear. A detailed balance study of the metabolites at widely varying levels of serum ascorbic is necessary to answer this question.

VOL.
5
1960/6

SUMMARY

Serum ascorbic acid levels and plasma hydrocortisone levels were determined in 12 normal subjects before, during, and after an experimental psychological stress (a hypnotically-induced anxiety state). The ascorbic acid levels of the subjects were unchanged across the four occasions of measurement with the female subjects' level about double that of the men. The hydrocortisone levels of the female subjects rose significantly during the anxiety period. The hydrocortisone levels of all subjects during the anxiety phase correlated highly with the ascorbic acid levels across all occasions. The conclusion that elevated ascorbic acid level was necessary for the secretion of increased amounts of hydrocortisone led to a second experiment in which

the plasma levels of ascorbic acid of a subgroup of the original population sample were increased by increasing the dietary intake of ascorbic acid. The serum ascorbic acid levels of these subjects were increased significantly and their hydrocortisone levels during the anxiety phase rose to higher levels than in the previous experiment.

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VOL.
5
1960/6

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YAWNING AND EPILEPSY*

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THIS communication reports observations made during an investigation into the emotional aspects of epilepsy indicating an association between yawning and anxiety and between yawning and spike and wave attacks in cases of petit mal epilepsy.

An association between petit mal attacks and yawning has not previously been reported in the literature, but an association between yawning and other types of epilepsy has been recorded, notably by Gowers [8], Wilson [14], Symonds [13] and Penfield [11]. A physiological study and review of the literature of yawning was done by Barbizet [1] and by Lasciewicz [10] in the normal and in association with certain tumours. Yawning was also observed in the case of an anencephalic monster by Gamper [6]. The psychological significance of yawning has received little attention and the biological significance of yawning is shortly discussed by Darwin in his *Expression of the Emotions in Man and Animals*. Apart from these references there are many unpublished clinical and common observations on the association of yawning with various states but few of them have been formally investigated.

In this study observations have been made on three patients during interviews totalling 97½ hr whilst recording the electroencephalogram (EEG), respiratory changes, psychogalvanic reflex (*PGR*) and pulse changes, these being recorded on magnetic tape and EEG paper simultaneously and correlated. The interview room and recording rooms were placed adjacently and separated by a one-way screen, the furniture being arranged so that the patient was under continuous observation from the recording room. All sounds were relayed from the interview room to a loudspeaker in the recording room, besides being recorded on magnetic tape and paper.

The significance of yawning was apparent towards the end of a series of experiments, and it become necessary in the assessment to total yawns and sighs together as noted on the record and also those estimated to be yawns by the waveform on the respiratory trace: this excluded any bias towards associating yawns with attacks because clinical details during attacks were more accurately noted than inter-attack periods.

The present report describes observations on three young girls suffering from epilepsy, being classical petit mal with 3 per sec spike and wave episodes on the electroencephalogram.

G. W. Aet 14, started attacks at 7 years. Her seizures were unresponsive to all forms of medication and occurred at the approximate frequency of 1 in 15 min, but they could drop to 2 per day. On physical examination nothing abnormal was detected in the central nervous system. She was a girl of passive personality and of average intelligence.

M. R. Aet 13, started her attacks at 8 years. Her attacks were refractory to drugs and occurred at the approximate frequency of up to 25 per day. She had a suspected lesion on the right side but this was not confirmed by spinal air-encephalogram, although the resting routine EEG showed an asymmetrical waveform. She was a cooperative and vivacious girl but liable to be overactive and provocative; she was of average intelligence.

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C. P. Aet 12, started her attacks at 10 years. Her seizures were refractory to drugs and had a very variable frequency of from none to 70 per day. On physical examination nothing abnormal was detected in her central nervous system apart from a slight asymmetry of her skull on the X-ray. She was a reserved, anxious, worrying girl liable to emotional outbursts at home; her intelligence was above average.

RESULTS

It was originally noted that yawning or sighing in one case (G. W.) occurred during electrical spike and wave attacks on the EEG, and also that they often started with or were preceded in the previous 20 sec by yawning or sighing thus showing a significant relationship between yawns and sighs and spike and wave attacks. It was also observed that when the interviewer (L. G.) left the room, the patients often yawned as he left, as he got up to leave, or just after he left the room: it was shown that in 3 cases there was a highly significant association between yawns or sighs and exits. In order to test the

TABLE 1.—COMPARISON OF YAWNS OR SIGHS IN DIFFERENT STATES

Patient	State	Yawns or sighs	Time hr, mins.	*P*	
G. W.	Associated with spike and wave attacks	80	2, 59	<0·001	Highly significant association with attacks
	Rest of recording	271	37, 7		
G. W.	Associated with spike and wave attacks	80	2, 59	<0·001	Highly significant association with attacks
	Silences and resting periods	31	7, 6		
G. W.	During spike and wave attacks	27		<0·01	Significant association with onset of attacks
	Associated with onset of attacks	53			
G. W.	Resting (O absent)	21	4, 2	—	Not significant
	Silence (O present)	10	3, 16		
M. R.	Resting (O absent)	5	3, 0	<0·001	Highly significant association with O being present
	Interview (O present)	78	25, 19		
G. W.	Exit of O	28	12⅓	<0·001	Highly significant association with exit of O
	Rest of recording	271	37, 7		
C. P.	Exit of O	12	9⅓	<0·001	Highly significant association with exit of O
	Rest of recording	23	23, 3		
M. R.	Exit of O	13	12	<0·001	Highly significant association with exit of O
	Rest of recording	83	28, 19		

VOL. 5 1960/6

relationship of yawns or sighs to these situations the experimental period was divided up into periods of silence (lapses in conversation of over 20 sec), conversation, spike and wave attacks and also a resting period when the patient was alone in the room. For present purposes the times were all added together to give the totals as shown.

On the null hypothesis that no relationships exist, it was assumed that two equal periods of time in specified situations were likely to contain equal numbers of yawns or sighs. The observed against the expected incidence of yawns or sighs was tested. Tests of significance were done comparing the observed proportions with an expected one of 0·5 using the arc sin transformation, described by Davies [5].

A comparison was made between yawns or sighs associated with attacks (i.e. those occurring during spike and wave attacks and also coincident with the 20 sec preceding the onset of spike and wave), and the rest of the time recorded. It was found that in one case (G. W.), 80 yawns or sighs were associated with attacks and occurred in 2 hr 59 min (attack time): during the rest of the time of recording, 37 hr 7 min, 271 yawns or sighs were recorded. The null hypothesis was that yawns or sighs would occur equally frequently in equal periods of time in "attack states" or "non-attack states". In this case the ratio of yawns or sighs in the two states was 80–20 and the null hypothesis was discarded at a very high level of significance ($P < 0{\cdot}001$). Bearing in mind that the figure for yawns or sighs occurring during conversation is an inflated one due to the possible miscalculation resulting from artefact when the patient was talking, it is safe to say that yawns or sighs occur most frequently here in association with the attack state. Another and more accurate comparison between yawning or sighing occurring in association with attacks (80 yawns or sighs in 2 hr 59 min) and those occurring during silences and resting periods (31 yawns or sighs in 7 hr 6 min) also showed that yawns or sighs were associated with attacks at a high level of significance ($P < 0{\cdot}001$).

Of the yawns or sighs associated with attacks (G. W.), 27 occurred during spike and wave attacks and 53 were coincident with the onset or the 20 sec preceding the onset of spike and wave. The null hypothesis was again applied to these two situations and showed that there was a significant relationship ($P < 0{\cdot}01$) that the yawns or sighs appear to occur rather more frequently associated with the period preceding and coincident with the onset of attacks than during attacks.

A comparison was made between periods when the patient was alone in the room and when the interviewer (O) was in the room but no conversation occurring. The total time of resting alone (G. W.) was 4 hr 2 min, during which 21 yawns or sighs occurred: the total time of silence, O being present, was 3 hr 16 min, during which 10 yawns or sighs occurred. The same hypothesis was applied and showed that the difference was insignificant. Since the periods of recording of the patient alone usually occurred at the beginning of sessions, this test also showed that there was no difference between the beginning of recording in this respect as opposed to the rest of the time of silence. This suggests that the patient is not more likely to yawn or sigh during silences because of fatigue or boredom than because of sleepiness at the commencement of a session.

A comparison was made between resting time when the patient was alone, and the interview time including silences when O was in the room. In one case (M. R.), yawns or sighs occurring in resting periods (O absent) (5 yawns or sighs in 3 hr) when compared with gross interview time (O present) (78 yawns or sighs in 25 hr 19 min) showed that

more yawns or sighs occurred when O was present than when he was absent and on the null hypothesis as above, at a very high level of significance ($P < 0{\cdot}001$).

There was a highly significant association between yawns or sighs and O leaving the room as shown in one case (G. W.), where 28 yawns or sighs occurred in association with 37 exits by O. If an average period of 20 sec is allowed for O to exit, yawns or sighs during recording time may be compared with those at exit of O, and on the null hypothesis as tested above, the results in all three cases are very highly significant ($P < 0{\cdot}001$) (G. W. where 28 yawns or sighs occurred during 12 min 20 sec exit time, compared with 271 yawns or sighs in 37 hr 7 min rest of recording time; C. P. where 12 yawns or sighs occurred during 9 min 20 sec exit time, compared with 23 yawns or sighs in 23 hr 3 min rest of recording; and M. R. where 13 yawns or sighs occurred in 12 min exit time, compared with 83 yawns or sighs in 28 hr 19 min rest of recording).

Yawns or sighs occurring in the 20 sec following a spike and wave attack were rare.

It should be noted that the interviewer, during these experiments, never yawned.

Only highly significant or relevant comparisons as tested on the null hypothesis that two situations do not differ, are shown.

DISCUSSION

Yawning is a complex physiological phenomenon according to Laskiewicz [10] divisible into slow, short yawning with widely opened glottis, and prolonged yawning in which the vocal chords are contracted and the glottis is tightened. The reflex has from antiquity been known to be influenced by psychical states and there are many observations on the association of paroxysmal yawning with certain pathological conditions [1]. Yawning is therefore a phenomenon which par excellence gives an indication of the influence of certain psychical states on centres in the nervous system subserving the yawning reflex.

It seemed worthwhile to report the observations on the association of yawning with certain alterations in state as there are so few references in the literature to objective studies of yawning as an accompaniment of psychical changes.

The yawning reflex is present from birth and has been observed in an anencephalic infant by Gamper [6]. Laskiewicz [10] in reporting two cases of cerebellar abscesses of otitic origin with "repeated and protracted yawning" and one with an acute supperative inflammation of the middle ear and "repeated and protracted yawning", reviews some of the published instances of its association with certain disease processes. Amongst these he mentions inflammatory processes and neoplasms in the posterior cranial fossa, especially cerebellar abscesses and abscesses of the internal auditory meatus; though inflammatory processes of the basal ganglia in the mesencephalon are said to be, unlike the cerebellum, rarely associated with yawning. Along with other authors, notably Barbizet [1], he notes the occurrence of yawning as a prelude to epileptic attacks. Gowers mentions yawning as a prodrome to epilepsy [8] and describes it in association with narcolepsy [7] and vagal attacks [9]; Wilson [14], Symonds [13] and Penfield [11] also describe instances of yawning as a prodrome to epileptic attacks. Philip Bard (personal communication) has noted that in chronic animal preparations after ablation of the cortex and certain other higher centres, yawning can still take place. D. A. K. Black (personal communication) noted protracted deep yawning during the experimental production of uraemic states by exsanguination in dogs, and a frequent association between paroxysmal yawning and uraemia and internal haemorrhage in humans. Other states are less clearly delineated, and include nausea, hunger, thirst and oxygen as found in unaired rooms and at high altitudes.

The reflex is subject to psychical influences and is generally taken to be an expression of weariness, exhaustion, anxiety or boredom, though one would not have expected opposite conditions such as boredom and anxiety to have the same effect. As an

VOL.
5
1960/6

expression of emotional states, little has been written on it. It has been noted in children (Platt, personal communication) that during psychotherapy when they have been told something they do not want to hear, they may yawn repeatedly: they may also do so when feeling extremely persecuted during or after temper tantrums.

Darwin briefly refers to yawning in his classic volume on *Expression of the Emotions in Man and Animals*, and mentions yawning in connection with weeping, since tears are frequently secreted. With fear he observed that there is a strong tendency to yawn. An interesting observation was on the expressive value of yawning in baboons who show their passion and threaten their opponents by opening their mouths widely as in the act of yawning, this action frequently leading to a real yawn. Some species of Macacus and Cercopithecus behave in a like manner and the hypothesis was advanced that the act served the purpose of showing an enemy a formidable set of teeth. Lasciewicz notes that yawning in humans can be produced by the imagination of, as well as the sight of a yawner, and also by long and anxious waiting. Yawning is notoriously infectious, probably more so than other mimical automatisms elicited by suggestion, such as laughing and weeping. These latter probably produce their effect by eliciting analogous psychic states. It may be conjectured that the highly infectious nature of yawning is not due simply to suggestion or mimicry but may be a more complex phenomenon due to the effect of the yawn, which may be seen as an expression of boredom or ennui.

In this communication an association between yawning, and, on the one hand a psychological situation, and on the other the onset of spike and wave attacks has been observed. It may be concluded that yawning is a low level reflex which can be evoked both by the presence of pathological lesions in the central nervous system and by toxic states, and is also well known to occur in certain psychological states. This study does not include observations on the biochemical alterations that probably result from psychical change, and themselves predispose to yawning, but one can speculate upon the biological significance of this universal reflex. Man in common with the rest of the mammalian species is possessed of a set of drives or needs which are partly innate and of physiological origin, and partly acquired as a result of early experience. His survival and health depends upon the gratification of these needs which include such basic factors as oxygen, water, food, sleep, excretion and warmth; on the other hand there is a need for affection, esteem, mastery and a sense of belonging. Non-gratification of such needs either of physiological origin or acquired origin arouses anxiety and it is in these conditions that yawning may occur. Thus for example yawning is seen in oxygen deficiency, either from environmental conditions (e.g. high altitude) or from pathological conditions (e.g. uraemia, cardiac failure) and is seen under conditions of thirst, hunger and sleep deprivation: it has however in humans a notoriously infectious quality. In these terms the occurrence of yawning in psychological states may superficially have the same meaning, that is a state of deprivation. A psychological change can be reflected in yawning, which in certain instances can be directly related to petit mal attacks. The significance of this for the precipitation of epilepsy is worthy of consideration.

SUMMARY

(1) In 3 epileptic patients, continuous recording of the E.E.G. and respiration and sound together with observation of the patients over long periods has been carried out.

(2) The periods of observation have been divided into periods of inactivity and periods during interviews.

(3) The occasions of yawns or sighs, and spike and wave episodes in the EEG have been correlated with the psychological status of the patients.

(4) A significant relationship has been found between yawning or sighing and the onset of spike and wave attacks on the one hand and between these and psychological stimulation on the other.

(5) Yawns and sighs occurred significantly more frequently during periods of stimulation than during periods of silence and inactivity.

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VOL.
5
1960/6

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SALIVARY SECRETION IN DEPRESSIVE ILLNESS*

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IN 1938 Strongin and Hinsie [1, 2] measured the Parotid secretion in psychiatric illness. They collected saliva with a Lashley suction cup attached to the orifice of Stensons's duct and found that depressed patients secreted saliva at a significantly lower rate than either manic patients or normal controls. Patients with a chronic schizophrenic illness salivated at a higher rate than normals.

These findings were next considered some twenty years later when Peck [3] collected saliva with cotton dental rolls left in the mouth for 2 min, and subsequently weighed them to find the amount of saliva absorbed. This very simple method (which Peck called the S.H.P. (Strongin, Hinsie, Peck) test was applied to groups of psychiatric patients, and a good correlation was found between clinical depression and reduction of salivary secretion. It was also found that normally the amount of saliva secreted tended to decrease in the morning, but was not affected by sex, age (between 20 and 60 years), or smoking habits.

Busfield and Wechsler [4] extended these observations with the S.H.P. test. Salivation rates were determined in 45 depressed hospitalized patients, 42 non-depressed hospitalized patients, and 50 normal controls. The depressed patients were found to salivate least and the normal controls most, though the severity of depression could not be correlated with the amount of saliva secreted.

In both the above papers the group labelled depressed included all subjects who had depressive symptoms irrespective of whether or not they had a depressive illness. The aim of the present investigation was to apply the S.H.P. test to subjects with clear cut depressive or schizophrenic illnesses. In addition it was intended to study the response of their salivation to stimulation by lemon extract. Preliminary studies also suggested that the method described by Peck might be conveniently modified as regards collecting and weighing the dental rolls.

MATERIALS AND METHODS

Subjects selected for testing were 30 consecutive female admissions, to the Bethlem Royal Hospital, with a diagnosis of a primary depressive illness made at the initial conference, whose subsequent course was consistent with this diagnosis: and 11 with a schizophrenic illness having symptoms of recent origin. 25 female members of the nursing and occupational therapy staff were used as controls. The groups were not matched for age since, as has been mentioned, Peck showed that this factor did not influence salivary secretion in the age range of these subjects (20–60 years).

Subjects were tested in the morning, at which time salivary secretion may be at a minimum [3]. No food, drink or sweets were allowed for one hour prior to testing. The previous night's hypnotics were given, but no other drugs were allowed for 24 hr before the tests. Dental cotton rolls 4 × 2 cm in size were used to absorb the saliva.

* From the Bethlem Royal and the Maudsley Hospitals, London, S.E.5.

Three rolls were placed in a waxed cardboard sputum cup, and the lid firmly screwed down, the total weight averaging 11 g. The weighings were carried out in conveniently large batches which were kept in the ward until use, without significant change in weight over three months. The relative lightness of the cups served to increase the accuracy of assessing the increment due to saliva.

The test was explained to each subject the day before to minimise anxiety. To ensure consistency, the same investigator did the testing procedure, the rolls being placed one on each side of the mouth against Stenson's duct, and one under the tongue.

After being left there for 2 min, they were then replaced in the sputum mugs and reweighed within 4 hr, during which time evaporation was found to be negligible. The weighing was done by a trained laboratory technician and was correct to 0·001 g.

The procedure was then repeated with the addition of two drops of a standard syrup of lemon extract placed on the tongue in order to stimulate salivary flow.

RESULTS

TABLE 1.—MEAN AND RANGE OF SALIVARY OUTPUT

Group	*N*	Resting levels (g)		Stimulated levels (g)	
		Means	Range	Means	Range
Depression	30	0·60	0·08–2·31	3·08	0·12–6·20
Schizophrenia	11	0·56	0·09–1·33	1·75	0·12–4·92
Normals	25	1·29	0·40–2·68	4·42	1·61–6·88

TABLE 2.—COMPARISON OF MEANS

Group		*t*	*P*
Depressed and normals	Resting levels	4·36	<0·01*
Depressed and schizophrenics		0·21	N.S.
Schizophrenics and normals		5·68	<0·01
Depressed and normals	Stimulated levels	3·12	<0·01*
Depressed and schizophrenics		2·07	<0·03*
Schizophrenics and normals		5·08	<0·01*

* Significant at 5 per cent level.

DISCUSSION

The results show that the S.H.P. test significantly differentiates between groups of patients with a depressive illness and normal controls: the latter producing the greater quantity of saliva. This holds also after salivary flow was stimulated by lemon extract. In addition it was found that within the depressed group, the test could not differentiate between the seven most and the seven least depressed patients.

The schizophrenic group showed, under resting conditions, results like those of the depressive, but after stimulation with lemon extract the schizophrenic group (seeming less able to respond), produced significantly less saliva than the depressed group.

While our findings in depression are similar to those of Peck [3] and Busfield [4], our results in schizophrenia are unlike those previously reported. In this respect it

VOL. 5 1960/6

may be noted that Strongin and Hinsie [2] studied schizophrenics whose chronicity distinguishes them from the patients admitted to this hospital. Busfield [4] used a diagnostic category "Schizo-affective depressed" which we believe insufficiently reliable to be useful.

Peck's aim of finding a physiological test which could be used to diagnose depression is, as he mentioned, not fulfilled by the S.H.P. test because of the overlap between groups. It also cannot be used to quantify the severity of depression. However it is still open to study whether it varies consistently with the progress of an individual depressive illness.

The results obtained after stimulation of the salivary flow differentiate significantly between the means of all three groups, and require further investigation. In particular the influence of drugs will have to be carefully controlled.

We agree with Peck [3] and Busfield [4], that the S.H.P. test is worth fuller study. It is known that normal variations in mood affect the salivary secretion [5, 6], and Peck [3] suggested that the reason that some of his depressed patients produced less saliva in the morning was the diurnal fluctuation in affect.

The S.H.P. test findings should be correlated with other physiological indices of autonomic activity in the individual patient. It may then be that certain patterns of autonomic activity could be correlated with specific clinical features or the therapeutic response of the patients to drugs or electroconvulsive therapy.

SUMMARY

Salivary secretion was measured by the S.H.P. test in groups of depressed and schizophrenic patients and in normal controls. The depressed and schizophrenic groups secreted significantly less saliva than normals. After salivary stimulation the schizophrenic group produced significantly less saliva than the depressives who in turn produced significantly less than normals. These findings are discussed and further studies suggested.

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HYPNOSIS IN BRONCHIAL ASTHMA*

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INTRODUCTION

THE opinion is widely held that psychological factors affect asthma [5, 4], and psychotherapy has been used in the attempt to help patients with this condition. Methods have included classical psycho-analysis [8], group therapy [10], manipulation of the emotional environment [13] and hypnosis [15, 6]. The last technique has been advocated with enthusiasm by some, but as a rule only anecdotal reports of its success have been available. When objective tests of respiratory function have been used, the results of hypnosis have often been disappointing. Thus Smith and Burns [15] found no objective evidence of improvement in 25 children after four sessions of hypnosis at weekly intervals. Edwards [6] found that the response to hypnosis of 6 patients with severe asthma was variable, and stressed the importance of distinguishing between psychological (subjective) and physiological improvement, which may not be comparable in degree in any one patient. The present study was undertaken to investigate further the immediate and long-term influence of hypnosis on the respiratory function and symptoms of adult asthmatic patients.

METHODS

Ten patients were studied. Five were females aged 29–57 years, and 5 were males aged 18 to 38 years. All patients were suffering from bronchial asthma with symptoms varying in duration from 18 months to 30 years (Table 1). In 6 patients (F3, F5, M6, M7, F8, M10) the condition could be classed as severe, having required repeated hospital admission. All but 2 (M2, F9) had been seen by a general physician, who had

TABLE 1.—CLINICAL DETAILS OF A GROUP OF 10 ASTHMATICS

Patient	Sex	Age (yrs)	Severity of asthma	Neurotic symptoms†	Duration of symptoms (yrs)	Months of treatment	Months of follow-up	State at end of trial		
								Activity	Subjective state	Drug consumption
F1	F	37	moderate	D	16	6	8	increased	improved	less
M2	M	38	mild	AT	30	4	8	unchanged	unchanged	unchanged
F3	F	32	severe	AD	2½	6	5	unchanged	unchanged	unchanged
M4	M	32	moderate	D	27	6	6	unchanged	unchanged	unchanged
F5	F	43	severe	D	8	6	6	increased	improved	less
M6	M	30	severe	A	15	8	6	increased	improved	less
M7	M	18	severe	AD	2	5	11	increased	improved	unchanged
F8	F	57	severe	A	4	6	7	increased	improved	unchanged
F9	F	29	mild	psychopathic personality	1½	3	0	—	—	—
M10	M	29	severe	A	21	7	5	increased	improved	less

† A = Anxiety: D = Depression: T = Tension.

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VOL. 5 1960/6

referred them for psychiatric advice: hence they form a group selected in the first instance for possible psychological disturbances. All except one (F9) were taking antispasmodic drugs when first seen, and 2 (F5, M6) were receiving corticosteroids.

At the first interview, a psychiatric case history was obtained, the proposed method of treatment outlined, and the patient's co-operation and consent to hypnosis secured. The apparatus used to determine respiratory function was then demonstrated, and brief training given in its use. The tests of respiratory function used were simple and easily repeated by the patient without undue fatigue. Vital capacity and mean expiratory flow rate were assessed with the patient in the sitting position, using a low inertia spirometer [2, 3]. Peak expiratory flow rates were measured with the flowmeter described by Wright and McKerrow [16]. The best of three successive results was recorded in each case. When antispasmodic drugs or corticosteroids were being used by the patient, the nature and quantity of these were noted, and the patient advised to continue taking them as prescribed by the physician in charge. No patient was tested within 2 hr of the last administration of a bronchodilator drug.

At the second and subsequent interviews, progress and drug consumption were noted, and respiratory function was assessed. Efforts were then made to induce hypnosis, with the patient lying in a semi-prone position. During hypnosis, easier breathing, lessening of tension and bronchospasm, and increase in confidence were repeatedly suggested to the patient. Each hypnotic session lasted between 20 and 30 min, and the depth of hypnosis was graded according to the following scheme:

Grade I—Relaxation and somnolence:

Grade II—Suggestibility as demonstarated by anaesthesia, levitation of limb, etc:

Grade III—Somnambulism, post hypnotic suggestion and amnesia.

On arousal the patient was returned to the sitting position, and his own assessment of whether his breathing was easier, worse or unchanged was recorded. After 2 min, tests of respiratory function were repeated.

In assessing vital capacity measurements before and after hypnosis, a change of 0·51 l. was arbitrarily regarded as significant. A change of 30 l. per min was shown to represent a significant change in consecutively measured expiratory flow rates in a population of asthmatics stabilized on antispasmodic drugs.

Six patients (F1, F3, F5, M7, F8, M10) were seen initially in hospital, but later joined the others as out-patients. From 7 to 10 sessions of hypnosis with each patient were undertaken over 4–6 months, and each patient was seen at intervals for a further period of 6–11 months. One patient (F9) withdrew from treatment after 3 months.

RESULTS

Psychiatric disorders found

It was not the main purpose of this work to investigate extensively the psychological background of each patient's illness. However factors emerged which seem relevant to the patients' response to the therapy used. All 10 patients had some mental disturbance. Patient M2 was referred in the first instance by his general practitioner because of marked tension and anxiety, related principally to his work, and impairing his efficiency at this. Anxiety was also prominent in 5 other patients (F3, M6, M7,F8, M10), and had resulted in considerable curtailment of their daily activities. Two men

(M6, M10) were unable to work because of anxiety, mainly expressed as fear of an impending attack of asthma, but also resulting in panic attacks when venturing far from home. Of the women, one (F3) was unable to go out shopping alone even when in remission from asthma, and another (F8) had changed from being an active member of surburdan society to a housebound hypochondriac.

Three patients (F1, M4, F5) had depression as the main psychiatric symption. This was most marked in patient F5, who was at one time suicidally inclined. Another man (M4) experienced considerable conflict and guilt over homosexual tendencies.

The remaining female (F9) had a psychopathic personality, with sexual promiscuity, barbiturate habituation, poor work record, and lack of moral sense as prominent features.

Immediate results of hypnosis (*Table* 2)

Eighty-two hypnotic sessions were undertaken, and it was possible to record respiratory function before and after 69. Optimum respiratory function for any patient may arbitrarily be regarded as the best level found during the study, since all patients were seen at times in remission from asthma. Thus objective improvement by hypnosis was only possible with certainty when breathing was impaired relative to this, which occurred on 56 occasions. In fact improvement in respiratory function occurred on 13. Breathing remained unchanged after 36 sessions, and deteriorated during 20.

The subjective responses were markedly different from the objective findings. After 51 hypnotic sessions patients felt that their breathing was better, no difference was felt after 26, and breathing was thought to be worse after 5. For the 69 sessions during which breathing tests were carried out, the figures were 40 improved, 25 unchanged and 4 worse. Of the 56 occasions when objective improvement could have occurred, subjective improvement was found in 37.

Table 2 also records data about the effectiveness of different grades of hypnosis in influencing tests of respiration.

TABLE 2.—THE EFFECT OF DIFFERENT GRADES OF HYPNOSIS

Hypnosis grade	Total number of sessions	Sessions with respiratory function tests	Sessions when objective improvement possible	Respiratory state after hypnosis*					
				improved		unchanged		Worse	
				O	S	O	S	O	S
0	7	3	3	0	1	2	3	1	3
I	22	17	13	5	15	8	7	4	0
II	41	37	31	5	28	19	11	13	2
III	12	12	9	3	7	7	5	2	0
Totals	82	69	56	13	51	36	26	20	5

* O = Objective state, S = Subjective state.

Grade I. Twenty-two sessions. Tests were carried out in 17. Patients' breathing was impaired before 13 sessions, and improved during 5. Eight produced no change, and respiration was further impaired after 4.

Grade II. Forty-one sessions, with respiratory function tests in 37. In 31, improvement was possible, but occurred only 5 times. Respiratory function deteriorated on 13 occasions, and remained constant on 19.

Grade III. Twelve sessions. Nine started with wheezing, and 3 showed improvement. Seven sessions resulted in no change, and 2 in deterioration.

Seven sessions failed to produce relaxation, and respiratory function tests were possible in 3 of these. Whilst all 3 could have resulted in improvement, none did so. Function was depressed after 1, and remained constant in 2.

The patients' subjective estimates of change in ease of breathing for each grade of hypnosis are recorded in Table 2. A similar proportion of hypnotic sessions of each grade were accompanied by symptomatic improvement. (Grade I, 15 out of 22; Grade II, 28 out of 41; Grade III, 7 out of 12).

A comparison of each individual's objective and subjective responses to suggestion is given in Fig. 1. Physiological improvement was usually accompanied by lessening of patients' dyspnoea as reported by them. When respiratory function deteriorated, over half the reports (11 out of 20) were again of increased freedom of breathing. Similarly, patients whose respiratory tests were unchanged often considered themselves improved (18 out of 30). Only one patient (F9) always correlated respiratory symptoms accurately with test results, neither being affected by hypnosis.

A departure from routine was made on several occasions, when temporarily increased spasm and dyspnoea were suggested to patients during the course of hypnosis. A record of one such instance is shown in Fig. 2 (M4). Both vital capacity and expiratory flow rate fell during the suggested asthmatic attack, and rose again as relaxation of bronchospasm was suggested.

Clinical course

At the end of the period of follow-up, 12–17 months from the beginning of the study, 6 patients thought they were better than at the onset of treatment (Table 1). Three thought there was no change, and one did not attend for review. The six who thought themselves improved showed increase in the range of their everyday activities.

Two men (M6, M10) had obtained regular work, having been unemployed for at least one year before starting hypnotherapy. One other (M7) was working full time having been undertaking only casual employment previously, and had again taken up dancing and swimming. One female patient (F1) had started once again to sing in a church choir—quite a severe test of respiratory efficiency, and 2 other women (F5, F8) were more active in their domestic and social lives.

These changes were accompanied or preceded by improvement in the affective symptoms noted at the beginning of the trial. Phobic anxiety had diminished in the men who obtained work, and was very much less in one of the women (F8). The original mood of depression had lightened in 2 women (F1, F5) and in one man (M7). Anxious introspection and tension were less in patient M2, who showed, however, no change either in asthma or in his capacity for sustained work and recreation.

No patient was free form bronchospasm and in no case were the results of repeated respiratory function tests during the follow-up period markedly different from those observed earlier.

The number of hospital admissions for the whole group during the year preceding therapy was 14. During the period of observation (12–17 months) a total of 4 hospital

admissions was required (F3 (twice), F5, M7). Three patients (F1, F5, M6) were using less bronchodilator drugs at the end of the trial than at the beginning. No patient was using more.

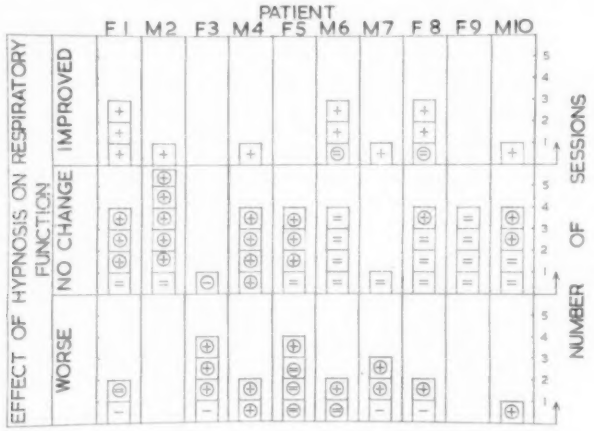

FIG. 1.—Effect of hypnosis on breathing in 10 asthmatic patients. Subjective changes are recorded thus: = (no change), + (improved), − (worse); Those differing from objective findings are ringed, thus: ⊕

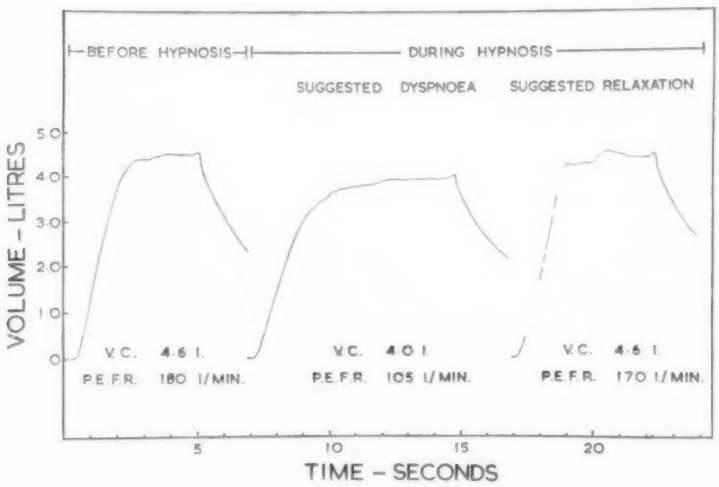

FIG. 2.—Changes in respiratory function tests induced under hypnosis.

DISCUSSION

This study provides no evidence that hypnosis consistently improves respiratory function in patients with asthma. Hypnosis in those patients whose breathing was impaired at the start of a session was followed by further deterioration (14 sessions) just about as often as improvement (13 sessions). In addition the tests of patients with optimum respiratory function beforehand showed deterioration after hypnosis on 6

occasions. Judged over a period of 12–17 months, no definite trend either way in patients' respiratory efficiency was observed. These findings are consistent with those of other workers who have objectively tested the results of hypnosis in patients with asthma.

In certain cases, however, it is reasonable to suppose that hypnosis modifies bronchospasm. Thus a causal effect was probable in those cases (e.g. M6) where suggested degrees of dyspnoea were accompanied by appropriate changes in respiratory function (Fig. 2).

It may be argued that the absence of objective improvement is a result of inadequate hypnosis, due either to poor technique or to patient resistance. In the field of dermatology, for instance, the cure of warts was impressively related to depth of hypnosis [14]. However, others have felt that deep hypnosis is not essential for relief of symptoms [1], and the present results support this. Thus, following 9 sessions of Grade III hypnosis, 3 patients improved, and after 13 sessions of Grade I hypnosis, 5 patients improved, the proportion being about the same for each level of hypnosis.

The frequent occurrence of deterioration after hypnosis requires explanation. It is known that the breathing of asthmatics changes from minute to minute, and both the deterioration and the improvement which were observed may have been due to the operation of chance. Other factors may have been concerned. Thus a change to the recumbent position is accompanied by a fall in vital capacity due to redisposition of blood and abdominal viscera, and hypnosis was carried out with the patient in a semi-prone position, which would allow such a change to occur. However, patients were tested in the sitting position, 2 min after hypnosis, when it is likely that the effects of recumbency on vital capacity would have ceased. During hypnosis, tidal ventilation diminished in some cases. This could be accompanied by functional closure of peripheral lung units, particularly in cases where bronchiolar and alveolar exudate were present, with consequent diminution in lung compliance and vital capacity in the period immediately following hypnosis. A similar increase in lung rigidity has been shown to occur even in normal subjects after a period of quiet breathing [7].

The disparity between subjective and objective response to hypnotherapy in asthma is perhaps the most striking feature to emerge from this work and was previously noted by Edwards [6]. Fig. 1 shows that all but one of the patients in the present study over-estimated improvement in response to hypnosis at some time or other. The reverse effect was rare, and only two patients (M6, F8) reported no change when tests revealed improvement, and only one (F3) reported deterioration when testing showed constant function. Indeed, only five reports of increased difficulty with breathing were obtained throughout the study. These consistent observations of subjective improvement must explain many of the good results attributed to hypnosis in this condition.

It seems most likely that the patients' optimism was due to post-hypnotic suggestion, manifest at a psychological level, but unable to penetrate to somatic effectiveness. One difficulty in accepting this view follows from the evidence, mentioned above, that all levels of hypnosis were followed by subjective improvement in about the same proportion of cases. Depth of hypnosis was assessed partly by the presence or absence of post-hypnotic suggestion, with respect to simple activities such as eye-blinking or number-forgetting, which were introduced specifically for testing purposes. By

definition, therefore, the effects of post-hypnotic suggestion should be less following the lighter levels of hypnosis. It may be that automatic activity, mental or physical, following hypnosis emerges with a facility dependent upon the intensity of suggestion directed towards it, in which case the threshold for respiratory effects would be reached before that for non-respiratory test activity. If so, more patients could be expected to report easier breathing than to show the comparatively weakly suggested post-hypnotic test activities.

Further confirmation that over-valuation of subjective improvement was a post-hypnotic phenomenon is given by the patients' assessment of their condition at the end of the trial. By this time, the transient effects of suggestion were no longer effective, and the patients' judgment was more in line with reality. Those that felt improved were in fact leading more active lives, although respiratory improvement where present was due to increase intervals between asthmatic attacks rather than to better respiratory function during remissions.

In view of the objective findings, it is perhaps surprising that 6 of the 10 patients derived benefit from hypnosis, judged by a comparison of activity before and at the end of the trial. It is felt that the explanation of this lies in the occurrence of depression, phobic anxiety and mixed neurotic states in this group (Table 1). A high incidence of such symptoms has previously been observed in a larger series [11]. Many asthmatics, it is suggested, are disabled not so much by difficulty in breathing as by their psychiatric illness. Modification of the latter may lead to increased effectiveness in patients who have already received the usual physical methods of treatment, as illustrated by the case histories outlined previously.

VOL.
5
1960/6

It is well recognized that suggestion is important in treating asthmatics, but in view of the lack of predictable effect on ventilatory function it is not justifiable to use this as the sole method of treatment. Bronchodilator drugs, corticoids and antibiotics may be indicated alone or in combination to prevent permanent lung damage and subsequent cardiac disability. It is however equally important not to ignore those emotional difficulties either inherent in the personality of asthmatic patients or secondary to their disease, which may potentiate symptoms of minor physical dysfunction so that these become disabling. This was recognized by Gillespie [9] who stated "So long as those who treat asthma fail to consider in every case when it first comes to their hands the possibility of psychological factors, so long will a number of people be turned to chronic invalidism". In this group, psychotherapy, including hypnosis, is of benefit, and should proceed concurrently with other treatment.

SUMMARY

Ten patients with asthma, referred for psychiatric opinion, were treated by hypnosis and later observed for 6–11 months. Respiratory function tests were carried out before and after hypnosis, and during the review period.

Although most patients reported improvement, hypnosis had no predictable effect upon respiratory function. Six patients became more active in work or social activities, and this was attributed to modification of neurotic attitudes.

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THE OCCURRENCE OF FOOD PREFERENCES AND AVERSIONS IN GROUPS OF PATIENTS WITH PEPTIC ULCER, ASTHMA AND NEUROSIS*

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INTRODUCTION

THIS study was planned after reading the publications of Wallen [9, 10] concerning food aversions. In these publications it was demonstrated that neurotic soldiers had more aversions to foods named on a list, than had normal soldiers. In the first group of 50 neurotics and 100 normals to whom the list of foods was read, the average number of aversions was 3·5 and 0·7 respectively; in the second group of 45 neurotics and 114 normals who had to complete the printed form of the list, the figures were 3·3 and 0·9. This difference was statistically significant. Gough [5] carried out similar researches using another group of soldiers. He compared 79 psychiatric patients in a military hospital (8 mild psychoneurotics, 27 moderate psychoneurotics, 35 severe psychoneurotics and 9 psychopathic personalities) with 254 normal soldiers. The same list of 20 foods was used which Wallen had applied in his research of 1945. In the group of neurotics the average number of aversions was 5·14, and in the group of normals an average number of 1·23 was found.

The tendency of neurotics to react with feelings of aversion to food is a symptom which is well-known to most psychiatrists, but it seems difficult to find a way to measure the intensity of this tendency. Wallen, however showed that it was possible to obtain some idea of that intensity, for the extent of the aversion in the different types of food gives in some degree a measure of it. This is the case because the aversions of neurotics fall into much the same pattern as the aversions of normal people. As Gough says, "Neurotics appear to dislike more foods, but not different foods, when considered as a group."

It appears, therefore, as if there were a certain threshold for aversion, which is lowered in neurotics. When, in Wallen's researches, the foods were arranged in descending order of aversion for neurotics and for normals, the rank order correlations between the lists was 0·75 if the questionaires were read to the subject, and 0·77 if the subject had to complete the printed form. Gough, who only gave his questionaire in the "oral" form, found a rank order correlation between the neurotics and normals of 0·82.

In view of these findings, we thought that it might be of interest to study the aversions and preferences of ulcer patients: for, if the hypothesis is correct that psychological factors play a role in the origin of peptic ulcer, peculiarities in the psychological meaning of foods might be expected. It is this psychological interpretation of food that will become evident in aversion or preference.

To obtain, sufficient insight into the situation of the ulcer patients it will be necessary to compare the findings obtained with regard to them with those from other patients.

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VOL.
5
1960/6

It will further be interesting to trace the correlation between the neurotic tendency and the tendency to aversion in these groups. Smith [8] had studied this correlation in a population of students using the Taylor Anxiety scale and a list of 29 foods. It was found that the high anxiety individuals had a greater number of food aversions than low anxiety individuals. An r of 0·174 ($P < 0·01$) was found between the number of anxiety-scale items checked and the number of foods disliked.

PROCEDURE

We gave all patients examined over the last few years in our department a list of 30 foods. They were asked to mark the foods for which they had an aversion. Of this list the first 20 items were almost the same as those used by Wallen with some changes to adjust it to Dutch circumstances. Ten foods were added which we expected would have a special meaning with regard to their colour, consistency or smell.

The following list was used:

Tea	Mushrooms	Milk
Grapefruit juice	Radishes	Coffee
Bean soup	Tomatoes	Red beets
Salmon	Melon or cantaloupe	Golden rennets (sour apples)
Rumpsteak	Cherries	Sweet apples
Veal chops	Pears	Vermicelli soup
Chicken	Mashed potatoes	Red cabbage
Fried eggs	New cheese	Spinach
Swiss cheese	Green cabbage	Shrimps
Broad beans	Oatmeal porridge	Mussels

Further on there was a list of 20 items of which the subject had to mark those he liked:

A glass of milk	Salt herring	Collared herring
Apple sauce	Old cheese	Smoking a cigar
Tea	Chicory	Smoking a cigarette
Ice-cream	Wine	Yoghourt
Coffee	Pea soup	Sauerkraut
Fried fish	Pancakes	Fried potatoes
Beer	Rum bonbons	

To ascertain whether the list of aversions and preferences had some reliability the split-half reliability of these lists was computed from the data of 100 patients with various illnesses. The split-half reliability of the aversions was found to be 0·65, that of the preferences 0·88. These correlations indicated that both lists had an acceptable internal consistency. In addition to the two lists, there were questions about the preferences and aversions to certain tastes and about appetite and feeding-habits. Of all these questions only two proved to be significant in connexion with this research:

"Are you often looking forward to meal time?"

"Do you generally enjoy your breakfast in the morning?"

Besides many other tests, our subjects were given a Dutch translation of the Maudsley Medical Questionnaire. This was chiefly a translation from the German version [3]. We tried to ascertain the correlation between the tendency to aversions and the neurotic tendency by comparing the checks on the aversion list and on the M.M.Q.

Our subjects had to complete the lists after reading them, but assistance was available to provide further information if this proved to be necessary.

SUBJECTS

At first we aimed at comparing groups of normals and of patients with neurosis, with peptic ulcer and with asthma. It was, however, impossible to compose a group of comparable normals. We had a group of 45 nurses of which the mean number of aversions was 2·78, but such a group cannot be compared with groups of patients. The ages of our subjects varied between 26 years and 62 years. With regard to the social status we classified all our subjects by means of the social level list standardized by the Institute of Social Research of the Netherlands Population. The groups were composed in such a way that the differences in age and social status of the groups were not statistically significant (see Table 1).

TABLE 1.—COMPOSITION OF THE GROUPS OF PATIENTS WITH REGARD TO AGE AND SOCIAL STATUS*

	Peptic ulcer	Asthma	Neurotics
Mean age, years	44·5	44·8	43·3
Mean social status	4·67	4·93	4·77

Peptic ulcer—Asthma:	Age, $t = 0{\cdot}10$; Social status, $t = 0{\cdot}39$
Peptic ulcer—Neurotics:	Age, $t = 0{\cdot}49$; Social status, $t = 0{\cdot}45$
Asthma—Neurotics:	Age, $t = 0{\cdot}25$; Social status, $t = 0{\cdot}25$

* All the groups contained 22 men and 8 women. With regard to age and social status the women of each group were comparable to the men.

As to the diagnosis, the neurotic patients all suffered from anxiety hysterical syndromes, in which stomach complaints held no important place. A complete clinical investigation revealed no abnormalities. All the patients in the asthma group had attacks observed in hospital; they had no other diseases and had no important degree of disability. In the peptic ulcer group, the ulcer was the only abnormality that could be found after clinical observation. The diagnosis of the ulcer depended on the finding of distinct abnormalities on radiological examination. Seventeen patients suffered from ulcus duodeni, and 13 from ulcus ventriculi. All the patients were observed in one of the two medical departments of the Municipal Hospital.

RESULTS

Patients with an ulcer and those with a neurosis had more aversion than those with asthma, but only the difference between peptic ulcer and asthma was significant at the 5 per cent level (Table 2).

TABLE 2.—OCCURRENCE OF AVERSION IN THE GROUPS

Peptic ulcer	Asthma	Neurotics
Mean = 3·87	Mean = 2·00	Mean = 3·30

Peptic ulcer—Asthma:	$t = 2{\cdot}17$; $P < 0{\cdot}05$
Peptic ulcer—Neurotics:	$t = 0{\cdot}57$; N.S.
Neurotics—Asthma:	$t = 1{\cdot}82$; N.S. (0·08)

Patients with ulcer and patients with asthma had more food preferences than neurotics; the difference between ulcer and asthma was significant at the 5 per cent level, thatbetween neurotics and asthma even at the 2 per cent level (Table 3).

VOL. 5 1960/6

The two questions regarding the appetite also showed that the asthma group and ulcer group had a more positive attitude towards food. Both questions were combined for statistical treatment. This is made possible by the fact that the two questions correlate in a group of 100 patients to a degree of 0·32 (Table 4).

TABLE 3.—OCCURRENCE OF PREFERENCES IN THE GROUPS

Peptic ulcer Mean = 11·65	Asthma Mean = 12·10	Neurotics Mean = 9·70

Peptic ulcer—Asthma:	$t = 0{\cdot}46$; N.S.
Peptic ulcer—Neurotics:	$t = 1{\cdot}97$; $P < 0{\cdot}05$
Neurotics—Asthma:	$t = 2{\cdot}43$; $P < 0{\cdot}02$

TABLE 4.—NUMBER OF 'YES' RESPONSES ON THE QUESTIONS: ARE YOU OFTEN LOOKING FORWARD TO MEAL TIME? DO YOU GENERALLY ENJOY YOUR BREAKFAST IN THE MORNING?

Peptic ulcer	Asthma	Neurotics
39	40	27

Peptic ulcer—Asthma:	$\chi^2 = 0{\cdot}037$; N.S.
Peptic ulcer—Neurotics:	$\chi^2 = 4{\cdot}850$; $P < 0{\cdot}05$
Neurotics—Asthma:	$\chi^2 = 5{\cdot}710$; $P < 0{\cdot}02$

TABLE 5.—RANK ORDER CORRELATIONS (RHO) OF AVERSIONS AND PREFERENCES AMONG THE GROUPS*

	Aversions	Preferences
Peptic ulcer—Asthma	0·50	0·67
Peptic ulcer—Neurotics	0·58	0·81
Neurotics—Asthma	0·64	0·60

* All significant at 1 per cent level.

We also investigated the rank order correlation of the aversions and preferences among the 3 groups (Table 5).

It might be possible that particularly for the ulcer patients there is a relation between the aversions and the fact that some foods give physical complaints. For this reason we asked all our subjects to name the substances that gave them stomach complaints. Some of the foods and beverages they named appeared on our aversion list. If we excluded them we got a list with the following items: tea, grapefruit juice, Swiss cheese, mushrooms, mashed potatoes, new cheese, oatmeal porridge, vermicelli soup, spinach, and shrimps. The total number of aversions against these 10 foods for each group is given in Table 6

The results obtained with this abbreviated list agree with the results obtained with the whole list. Food aversions of ulcer patients cannot therefore simply be reduced to the physical effects of food.

As we have seen before the rank order of the aversions and of the preferences is much alike in the different groups, but beer and wine from the preference list held a particular place. Though there was no important difference between the number of

preferences and of the asthma group and the ulcer group, we found a significant difference between the preference for wine and beer in these groups. Table 7)

It seems interesting to examine in what way appetite (as measured by the two questions named before), aversions, and preferences were interrelated. Table 8 illustrates the correlation between the variables.

TABLE 6.—TOTAL NUMBER OF AVERSIONS ON 10 ITEMS OF THE AVERSION LIST, WHICH HAD NOT GIVEN PHYSICAL COMPLAINTS

Peptic ulcer	Asthma	Neurotics
38	23	45

Peptic ulcer—Asthma:	$\chi^2 = 3{\cdot}93$;	$P < 0{\cdot}05$
Peptic ulcer—Neurotics:	$\chi^2 = 1{\cdot}02$;	N.S.
Neurotics—Asthma:	$\chi^2 = 8{\cdot}07$;	$P < 0{\cdot}01$

TABLE 7.—NUMBER OF PREFERENCES FOR BEER AND WINE

Peptic ulcer	Asthma	Neurotics
13	26	15

Peptic ulcer—Asthma:	$\chi^2 = 4{\cdot}11$;	$P < 0{\cdot}05$
Peptic ulcer—Neurotics:	$\chi^2 = 2{\cdot}09$;	N.S.
Neurotics—Asthma:	$\chi^2 = 1{\cdot}14$;	N.S.

TABLE 8.—CORRELATION (r) BETWEEN APPETITE, AVERSIONS AND PREFERENCES IN THE GROUPS OF PATIENTS*

	Peptic ulcer	Asthma	Neurotics	Total
Appetite—Aversions	−0·29	−0·27	−0·47	−0·34
Appetite—Preferences	+0·30	+0·32	+0·55	+0·39
Aversions—Preferences	−0·48	−0·28	−0·32	−0·36

* For $N = 30$, significance level at 5 per cent = 0·361
For $N = 30$, significance level at 1 per cent = 0·462
For $N = 90$, significance level at 1 per cent = 0·266

TABLE 9.—CORRELATION (r) BETWEEN AVERSION AND NEUROTIC TENDENCY AS MEASURED BY THE M.M.Q.

Aversions—M.M.Q. = 0·090	[Asthma	$N = 74$	(40 M + 34 W)]
Aversions—M.M.Q. = 0·190	[Peptic Ulcer	$N = 74$	(53 M + 21 W)]
Aversions—M.M.Q. = 0·265	[Thyrotoxicosis	$N = 30$	(3 M + 27 W)]
Aversions—M.M.Q. = 0·260	[Neurotics	$N = 43$	(26 M + 17 W)]
Aversions—M.M.Q. = 0·194	[Totals	$N = 221$	(112 M + 99 W)]

Though not all correlations are significant, the trend in the 3 groups is the same. If we combine the correlations obtained for the 3 groups separately (as is possible in this case, because the correlations do not vary much), all the correlations are significant at the 1 per cent level.

We also tried to correlate the number of aversions with the tendency to neuroticism.

The M.M.Q. was employed for this purpose. As it was not our aim to compare the groups, we used larger numbers of patients in each group, but we took the same precautions with regard to the diagnoses as has been mentioned previously (Table 9).

VOL.
5
1960/6

Of the 38 questions of the M.M.Q., 11 directly relate to physical health and complaints, (corresponding with questions 1, 4, 17, 30, 35, 36, 46, 47, 49 and 50 and 53, in the German version). We thought that it might also be interesting to investigate the correlation between the aversions and the M.M.Q. from which these 11 questions were removed (Table 10).

TABLE 10.—CORRELATION (r) BETWEEN AVERSIONS AND ITEMS CHECKED UPON THE M.M.Q. FROM WHICH THE QUESTIONS ABOUT PHYSICAL HEALTH ARE REMOVED

Aversions—M.M.Q. = 0·129	[Asthma	$N = 74$	(40 M + 34 W)]
Aversions—M.M.Q. = 0·159	[Peptic Ulcer	$N = 74$	(53 M + 21 W)]
Aversions—M.M.Q. = 0·267	[Thyrotoxicosis	$N = 30$	(3 M + 27 W)]
Aversions—M.M.Q. = 0·296	[Neurotics	$N = 43$	(26 M + 17 W)]
Aversions—M.M.Q. = 0·197	[Totals	$N = 221$	(112 M + 99 W)]

From Tables 9 and 10 we can infer a low but consistent relation between neuroticism measured by the M.M.Q. and the number of aversions. The average correlation for the four groups is of the same magnitude as that found by Smith [8]. The combined correlation is significant at the 1 per cent level of significance for this number of subjects.

DISCUSSION

As already mentioned we found a small correlation between the M.M.Q. and the number of aversions. It is known that the M.M.Q. has a loading on the factor of neuroticism [2], and as a result we may say that our findings confirm those of Wallen [9] and Gough, [5], who by comparing the number of aversions in a group of normal and in a group of neurotic subjects, found a relation between neuroticism and food aversions.

The ulcer patients as a group have practically speaking the same high tendency to aversions as have neurotic subjects, but they also have a high tendency to preferences, while the latter is low in neurotic patients.

In the individual ulcer patient, there is, however, a negative correlation between aversions and preferences, so that a patient with more aversions has generally speaking fewer preferences than an ulcer patient with fewer aversions. However, he has probably more preferences and more appetite than a neurotic patient with the same tendency to aversion.

Comparing the group of ulcer patients with neurotics and asthma patients one can say that the ulcer patient has a more ambivalent attitude to food than the other. Though we realise that our groups are too small to reach definite conclusions, we still think that the findings indicate that it might be possible to differentiate in this way ulcer patients from the neurotic patients and from asthma patients. We hope it will be possible to repeat such a research in the future with a larger material.

Alexander [1], Groen [6], and Goldberg [4] have demonstrated the influence of the psychological meaning of the social circumstances in the causation of peptic ulcer. Aversion is not restricted to food, but can extend to other objects and situations in life, so well shown in the novel *La Nausée* by J. P. Sartre [7]. On the other hand we all know of preferences for objects that have nothing to do with eating, and which are expressed in an oral way. With this in mind it would be interesting to try to investigate by statistical methods not only the tendency to aversion and to oral preference toward food, but also toward life-situations.

It is also possible to connect our findings with the somatic aspect of the causation of the peptic ulcer. Aversion and appetite are the two possible attitudes to food. The physiological reactions connected with appetite are very distinct from those connected with aversion. If aversion and appetite come close to each other there is a great danger that those physiological mechanisms are intermingling and that the somatic process does not have its natural course. It would not be surprising that such disturbed physiological reactions should finally lead to disturbances. If we put it in this way we can say that the attitude of the ulcer patient to his food is very specific and dangerously exclusive. Perhaps this is not only the case with his attitude to food, but also with that to other situations in his life.

SUMMARY

The attitude to food was studied in three groups of patients (patients with neurosis, bronchial asthma, and peptic ulcer) by giving them a check-list on which they had to mark the foods against which they had an aversion, another list for the preferences and a number of questions of which two, both connected with the appetite, proved to be important.

The neurotic group showed many aversions, few preferences and little appetite. The asthma group showed few aversions, many preferences and a good appetite. The ulcer group had a more ambivalent attitude, many aversions, many preferences and a good appetite.

Furthermore, the correlation between the neurotic tendency measured by the M.M.Q. and the number of aversions in a larger group of patients was investigated; a small correlation was found.

An attempt was made to bring the observed facts into relation with other data derived from psychosomatic research on peptic ulcer.

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VOL.
5
1960/6

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VOL.
5
1960/6

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BOOK REVIEWS

A. N. LEONT'EV and A. V. ZAPOROZHETS. **Rehabilitation of Hand Function.** (Translated by BASIL HAIGH and edited by W. RITCHIE RUSSELL.) Oxford: Pergamon Press. 1960. Pp. xiii + 199; illustrated. 60s

THIS book was first published in Russia in 1945 and reports the efforts that were made there to improve the rehabilitation of those who sustained hand injuries during the War. It endeavours to place occupational therapy on a scientific footing and to discover means by which the greatest use can be obtained from injured hands.

The authors stress the importance of psychophysiological mechanisms and the effect on movement of the emotional attitude of the patient. They feel it a necessity that the work performed should be productive and that repetitive tasks or even basketry serve to emphasise a disability and are regarded by patients as "work for cripples". They consider that injury creates a disturbance in the proprioceptive field which affects co-ordination of movement, and that the afferent aspect of injury is of considerable importance. Throughout the book there are aphorisms summarising the points which have been illustrated by case histories and, as far as possible, verified by means of simple apparatus.

The highly organised forms of occupational therapy might be more easily applied in this country to service personnel than to the civilian population, but there are lessons to be learnt from the experience recorded here, and many of the principles enunciated need careful consideration. There is a useful summary of the main methods of occupational therapy employed.

Unfortunately, the price of this book is high owing to the cost of translation and production, and it was necessary to use a photolithographic process instead of the usual type in order to facilitate publication. There is a bibliography but no index. It should, however, be read by all those who are engaged in the rehabilitation of the injured.

PETER H. SCHURR

J. HERZOG-DÜRCK: **Menschsein als Wagnis. Neurose und Heilung im Sinne einer personalen Psychotherapie.** Klett, Stuttgart, 1960. pp. 300. D.M. 19·50.

THIS book presents "personal psychotherapy" as the natural evolution from analytic method, and philosophic thought. The author explains that healing neurotic illness implies over-coming the barriers which such illness imposes between the patient and existence. The patient in the healing process learns to accept the "fundamental conditions", such as death, sin, love and transcendence of the narrow boundaries of the immediate personality. In this process the therapist stands by the patient as a co-existent human being, the analytic method or contemplation of phenomena such as dreams being chosen as the existing situation seems to warrant. The therapist therefore must not only be fully conversant with analytic theory and practice, but must also be well-versed in the whole heritage of philosophy. Christian conceptions emerge inevitably from such work with the patient.

The author recognises four primary neuroses. Firstly, the patient who has failed to experience protective mothering in childhood, who then has no means of combating the fears of death and loss in life, and tends to develop a depressive neurotic illness. Secondly, the patient who was unable to relate to a stimulating, educating, supportive father-figure in childhood and who tends in later life to protect himself by obsessive/compulsive symptoms, which narrow his existence more and more. The hysteric, according to this author, has been unable to experience the combined and balanced functioning of both parents, and learns early to manipulate all situations to his advantage. Lastly, the schizoid personality has never, during childhood, experienced any feelings which bound him to other human beings.

EVA FROMMER

VOL.
5
1960/6

R. S. ILLINGWORTH: **The Development of the Infant and Young Child—Normal and Abnormal.** 1960. E. and S. Livingstone Ltd., Edinburgh and London. pp. viii + 318. 27s. 6d.

THIS is a valuable book on the motor and intellectual development of children; there can be very few paediatricians who would not be better informed by reading it. It is illustrated by 95 photographs, many of high technical and human quality. Professor Illingworth studied with Arnold Gesell and this book presents Gesell's methods of assessing developmental progress as Illingworth now uses them after many years of assessing and watching children.

Professor Illingworth emphasises that "it matters a great deal for the purposes of adoption, if the child's developmental quotient, being 70 or less, gives a reasonably likely prediction that the child is going to be mentally retarded in later years." He has shown clearly that it is possible to recognise moderate as well as severe intellectual handicap in infancy and since this is so, all adopting parents should have the child examined at the time of formal adoption (which cannot be less than the age of 3 months and will often be some months more) by someone with special experience in the examination of infants. Only in this way can various tragedies be avoided.

The book is enriched by summaries of many papers; of which one sometimes feels a critical judgment from someone with the author's erudition and experience would be helpful; at others one is rather surprised that Professor Illingworth is so dogmatic.

There is an excellent review of pre-natal and perinatal factors and of the effects of physical illness and defects on the child's development. The chapter on environmental factors and development covers a wide ground and includes a great deal of information but here especially one would have liked to know Professor Illingworth's own views on how the child's inherent potentialities react with his environment to produce his personality, and one would have liked this chapter to be more concerned with love and anger, and how the child's reactions to other people affect his behaviour, his learning and his personality; the more so as we know that Professor Illingworth can write with warmth and humanity. The nature of the relationship between the infant and his mother is not discussed and the important review of this by Bowlby ("The Nature of the Child's tie to his mother," BOWLBY J. 1958 *Int. J. Psychoanal.* **39,** 350) is not mentioned. Illingworth may well have deliberately eschewed such theoretic analysis but the observations of Harlow, Hinde, Levine and Tinbergen do so illuminate the learning and development of infants that they deserve to have been mentioned.

All good paediatricians will read this book; the rest of us need to read it and will be greatly benefited if we do. It will be a book of reference that we all should have in the Infant Welfare Clinic, in the Outpatient Department and in the Ward for frequent consultation.

RONALD MAC KEITH

Essays in Individual Psychology. Edited by KURT A. ADLER and DANICA DEUTSCH. Grove Press, Inc. Evergreen Books Ltd., New York, London. 1960. Pp. 480. 21s.

ALFRED ADLER'S followers can rightly claim that he foreshadowed not only important concepts of present day social psychology and psychiatry, but also some notions of ego psychology, which have been to the fore in psychoanalysis during the last three decades. However, it is difficult to say how much Adler's writings have directly contributed to these developments. His concepts have undergone hardly any changes since they were first advanced. It is more than fifty years since "social feeling" or "community sense" was proclaimed as the guiding principle of human behaviour. Only some of the contributors to this volume express Adlerian concepts in terms of modern social psychodynamics. Sartre's psychology is claimed to be fundamentally Adlerian. Group psychotherapy, psychodrama and sociometry can be viewed from the Adlerian point of view, although his concepts require a good deal of elaboration and amplification to do justice to the complexity of social interactions. Adler's negative attitude to the biological approach has made his basic concepts unacceptable to most medical psychologists, who would nevertheless acknowledge his contributions to the study of social behaviour. These essays by fifty psychiatrists and psychologists, published on the occasion of the tenth centenary of the Alfred Adler Clinic in New York, give a full picture of Adler's theory and its applications as practised today.

E. STENGEL

JAMES HILLMAN: **Emotion: A Comprehensive Phenomenology of Theories and Their Meanings for Therapy.** London, Routledge and Kegan Paul. 1960. pp. 318. 40s.

EMOTIONS are of crucial importance for many issues of medicine, psychotherapy and social life. Yet psychologists have failed to evolve a single theory which is universally applicable to the manifold aspects of emotional manifestations, their nature, causation and significance.

The author, who is the director of studies at the C. G. Jung Institute, Zurich, set himself the task of remedying this defect when he wrote his Ph.D. Thesis from which the present book took its origin. His plan was to use a phenomenological approach first and to integrate afterwards the data, thus obtained, with the help of a conceptual model comprehensive enough to encompass them all. The phenomenology used was a variant of Husserl's existentialist doctrine. Instead of going "right to the things themselves", the author went right to the theories and speculations of philosophers, psychologists, physiologists and many other writers on emotion. This he called the phenomenology of theories. He cast his net wide, surveying English, French, German and Spanish sources, and ranging from ancient metaphysicians and early Christian Fathers to modern scientists and clinicians.

The views of almost 500 writers are presented in a lucid and readable style, interspersed with many original quotations. The work has thus become a useful guide and reference book through the winding highways and by-ways of theories on emotion which often cover the same semantic ground, though apparently following differently labelled signposts.

There are some authors for whom emotions are only "intervening variables", but a majority speak of them as if they were specific forces, of a vitalistic or physical kind, occurring spontaneously or evoked by instincts and adaptations to stress. To "explain" psychiatric and psychosomatic symptoms, a deviation or blocking of these hypothetical forces is often assumed, and from such premises the beneficial effects of emotional catharsis, abreaction, exorcism and shock treatment deduced. Emotions are also variously interpreted in terms of conscious and unconscious processes; as phenomena ranging from shallow superficiality to the innermost depth of a person; as physiological activities localized in particular structures of the brain, or in the blood, the gut, the glands or the muscles; as responses to situations, stimuli, thoughts, memories or conflicts; and in a variety of other ways.

The author classified this "pandemonium of theory", as he aptly called it on one occasion, into nineteen arbitrary and overlapping types of theory. His purpose was to demonstrate the profusion and confusion of thought, and to replace it by a master theory of his own. In this final integrative effort, however, his easy style disappeared, making way for an abstruse presentation of yet another type of theory. His solution adopted and adapted the Aristotelian doctrine of causation. Aristotle's four causes (causa efficiens, materialis, formalis, and finalis) were extolled as providing an *a priori* and exhaustive model of causal explanation because the "fourfold root" was a self-evident (sic) symbol of completion and fulfilment which provided other "eminently satisfying and perpetually recurring explanations", such as the four humours of Hippocrates; the four directions, phases of the moon, elements and seasons; the fourfold religious mandalas; the four-legged mythological beast on which the world rests; and the four letters used ubiquitously (sic) for the name of God.

Such number mystique is poor evidence for the excellence of any explanatory model. It can be—and has been—used to point to the virtues of every number from one to thirteen, and for several higher numbers as well, including the infinite. Such an exercise in scholastic ingenuity provides a disappointing end to an otherwise enjoyable and informative book.

F. KRÄUPL TAYLOR

Pergamon Press. Catalogue of Scientific and Technical Publications. Pergamon Press. Oxford. 1961.

THE achievements of the Pergamon Press in the thirteen years since its foundation are already legendary. The recent 1961 catalogue makes fascinating reading—space research, mental deficiency, mining engineering, childbirth and almost every aspect of science figure among the publications. Copies may be obtained from the Pergamon Press, Headington Hill Hall, Oxford.

DENIS LEIGH

VOL.
5
1960/61

Verfolgung und Angst in ihren leib-seelischen Auswirkungen. (Psychosomatic sequelae of persecution and anxiety). Edited by HANS MARCH. Stuttgart, Ernst Klett. 1960. pp. 273.

IT IS now generally accepted that mental traumata suffered collectively have not the same pathogenic effects as those suffered by individuals alone. However, there are indications that this rule did not apply to the kind of traumatic experiences to which the victims of racial and political persecution were exposed in Germany before and during the last war. Even though they suffered with others, attitudes of collective resistance were never allowed to develop. Their situation in the society which was dominated by their persecutors, was fundamentally different from that of members of a population at war. This book is a collection of reports on patients who as the result of persecution and ill-treatment in concentration camps had become neurotic or psychotic, or had developed psychosomatic symptoms, such as bronchial asthma or hypertension. The authors of those reports, most of which were submitted to German courts in support of compensation claims, are distinguished German psychiatrists. The exceptional nature of the physical and psychological assaults made it appear highly probable that they had caused or had contributed to chronic mental and psychosomatic diseases. Reading the records of perverse acts of aggression one wonders what effects they might have had on the aggressors, not all of whom could have been abnormal personalities from the start. There have so far been no publications on this aspect of collective aggressive behaviour.

E. STENGEL

JAMES FARNDALE: **The day hospital movement in Great Britain**. Pergamon Press, Oxford, pp. xvii + 430, 84s.

SOVIET RUSSIA has employed day centres in connection with neuropsychiatric services since 1942—Canada and Great Britain introduced day hospitals to the English speaking world in 1946. Since then the movement has slowly grown so that now at least forty such centres exist in Great Britain and about 1100 day places are available daily for patients. The protagonists of the Day Hospital movement claim that there are definite advantages in treating a patient half way, as it were, between home and hospital. Contact with the social milieu is maintained, the danger of institutionalisation diminished, and treatment is carried out more economically.

In this book Mr. Farndale describes the facilities provided by existing day hospitals and centres in Great Britain, and analyses the various administrative problems posed by the development of this comparatively new institution. The medical aspects are somewhat controversial and have yet to be fully and critically considered; being by profession a hospital administrator Mr. Farndale wisely expresses no personal views on these aspects. His book is a 'must' for all medical administrators and provides an invaluable source book of information on the present state of the Day Hospital in Great Britain.

DENIS LEIGH

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ANNOUNCEMENT

Conference on the Role of Psychosomatic Disorders in Adult Life

THE Society for Psychosomatic Research will be holding their third annual conference on aspects of psychosomatic medicine in various age groups. The first two conferences dealt with paediatrics and adolescence, and this year it is intended to provide a forum for the discussion of psychosomatic aspects in adult life.

Individual papers will be kept short, and the numbers participating will be limited to about one hundred, in order to permit general discussion, and to provide an intimate and informal atmosphere.

The conference will be held at the Royal College of Physicians, Pall Mall East, London, W.1, on Friday 3rd and Saturday 4th November, 1961. A dinner at the Royal College of Physicians will be arranged, to which guests will be welcome.

Those interested in attending this conference should write to:

Dr. H. H. WOLFF
Hon. Secretary
The Society for Psychosomatic Research
70, Harley Street
London, W.1

VOL.
5
1960/61

L.
/61